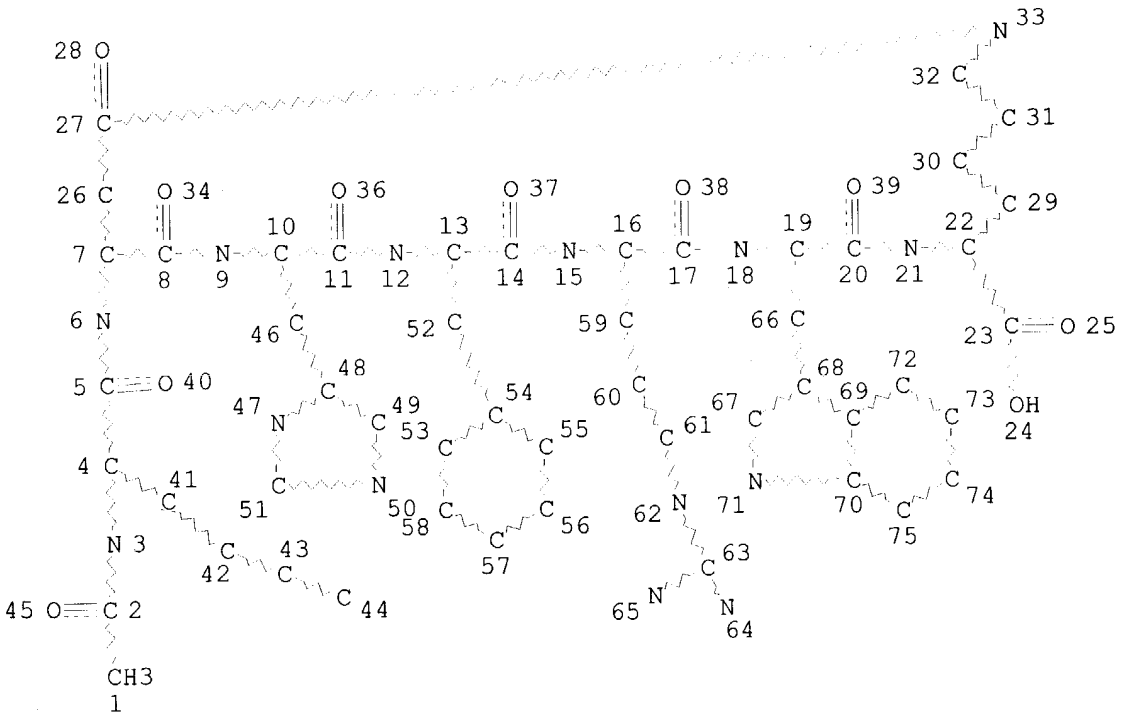
=> d que l12
L9 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 74

STEREO ATTRIBUTES: NONE
L11 1 SEA FILE=REGISTRY SSS FUL L9
L12 5 SEA FILE=HCAPLUS L11

=> fil reg
FILE 'REGISTRY' ENTERED AT 14:57:58 ON 19 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 18 MAY 2004 HIGHEST RN 683203-75-0
DICTIONARY FILE UPDATES: 18 MAY 2004 HIGHEST RN 683203-75-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 15:04:59 ON 19 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 19 May 2004 VOL 140 ISS 21
FILE LAST UPDATED: 18 May 2004 (20040518/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d ti rn l12 1-5

L12 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
TI Peptide composition for treatment of sexual dysfunction
RN 9068-52-4
RN 37213-49-3
RN 168482-23-3
RN 646031-08-5P
RN 646031-09-6P
RN 646031-10-9P
RN 646031-11-0P
RN 646031-12-1P
RN 646031-13-2P
RN 646031-14-3P
RN 646031-15-4P
RN 646031-16-5P
RN 646031-17-6P
RN 646031-18-7P
RN 646031-19-8P
RN 646031-20-1P
RN 58-22-0
RN 139755-83-2
RN **189691-06-3**
RN 143824-77-5

L12 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
TI PT-141: a melanocortin agonist for the treatment of sexual dysfunction

Search completed by David Schreiber x22526

RN 60-92-4
RN 37213-49-3D
RN **189691-06-3**

L12 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
TI Pharmaceutical compositions containing a peptide for treatment of sexual dysfunction
RN **189691-06-3**
RN **189691-06-3D**
RN 8012-39-3

L12 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
TI Compositions and methods for treatment of sexual dysfunction
RN 4289-02-5
RN 31008-44-3
RN **189691-06-3**

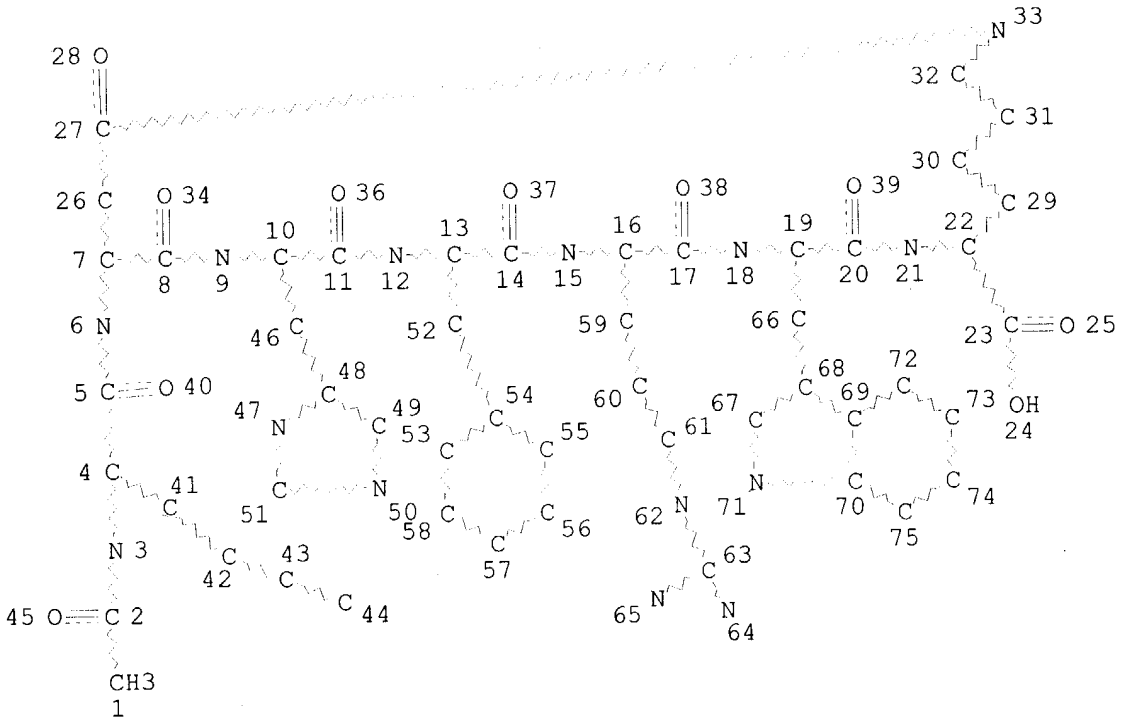
L12 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
TI Biological and Conformational Examination of Stereochemical Modifications Using the Template Melanotropin Peptide, Ac-Nle-c[Asp-His-Phe-Arg-Trp-Ala-Lys]-NH2, on Human Melanocortin Receptors
RN 581-05-5
RN 75921-69-6
RN 163560-08-5
RN **189691-06-3**
RN 189691-08-5
RN 189691-11-0
RN 189691-13-2
RN 189691-15-4
RN 60-92-4

Search completed by David Schreiber x22526

```
=> d his 1

     (FILE 'MEDLINE, HCAPLUS, WPIDS' ENTERED AT 14:32:33 ON 19 MAY 2004)
L15          28 DUP REM L6 L12 L14 (7 DUPLICATES REMOVED)

=> d que l15
L1           196 SEA BLOOD C?/AU
L2           114 SEA SHADIACK A?/AU
L3          4983 SEA BERNSTEIN J?/AU
L4           237 SEA HERBERT G?/AU
L5          5505 SEA (L1 OR L2 OR L3 OR L4)
L6             6 SEA L5 AND (CYCLIC? OR CIRCUL?)(3A) PEPTID?
L7           134 SEA FILE=REGISTRY 'NLE'DH.RWK/SQSP
L9               STR
```



```
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  74

STEREO ATTRIBUTES: NONE
L11            1 SEA FILE=REGISTRY SSS FUL L9
L12            5 SEA FILE=HCAPLUS L11
L13          224 SEA FILE=HCAPLUS L7
L14           24 SEA FILE=HCAPLUS L13 AND (CYCLIC? OR CIRCUL?)(3A)PEPTID?
L15           28 DUP REM L6 L12 L14 (7 DUPLICATES REMOVED)


=> d ibib abs hitstr l15 1-28
```

L15 ANSWER 1 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:41502 HCAPLUS
DOCUMENT NUMBER: 140:105305
TITLE: Peptide composition for treatment of sexual dysfunction
INVENTOR(S): Sharma, Shubh D.; **Shadiack, Annette M.**; Yang, Wei; Rajpurohit, Ramesh
PATENT ASSIGNEE(S): Palatin Technologies, Inc., USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005324	A2	20040115	WO 2003-US21417	20030709
WO 2004005324	A3	20040325		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-394756P P 20020709
OTHER SOURCE(S): MARPAT 140:105305
AB Peptides for treatment of sexual dysfunction, including erectile dysfunction and female sexual dysfunction, and combination drugs and method of use thereof, including a peptide of the invention and one or more second sexual dysfunction pharmaceutical agents are disclosed.

L15 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2003:58220 HCAPLUS
DOCUMENT NUMBER: 138:117676
TITLE: Linear and **cyclic** melanocortin receptor-specific **peptides**, and therapeutic use
INVENTOR(S): Sharma, Shubh D.; **Shadiack, Annette M.**; Yang, Wei; Rajpurohit, Ramesh
PATENT ASSIGNEE(S): Palatin Technologies, Inc., USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003006620	A2	20030123	WO 2002-US22196	20020711
WO 2003006620	A3	20031127		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

Search completed by David Schreiber x22526

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-304836P P 20010711
OTHER SOURCE(S): MARPAT 138:117676

AB Linear and **cyclic peptides** are provided which are specific to melanocortin receptors and which exhibit agonist, antagonist, or mixed agonist-antagonist activity. The peptides of the invention may be used to treat e.g. erectile dysfunction and eating disorders.

L15 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:133936 HCAPLUS
DOCUMENT NUMBER: 138:180744
TITLE: Compositions and methods for the diagnosis and treatment of psychogenic erectile dysfunction
INVENTOR(S): Mann, Morris; Mann, Maria A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003036514	A1	20030220	US 2002-198793	20020718

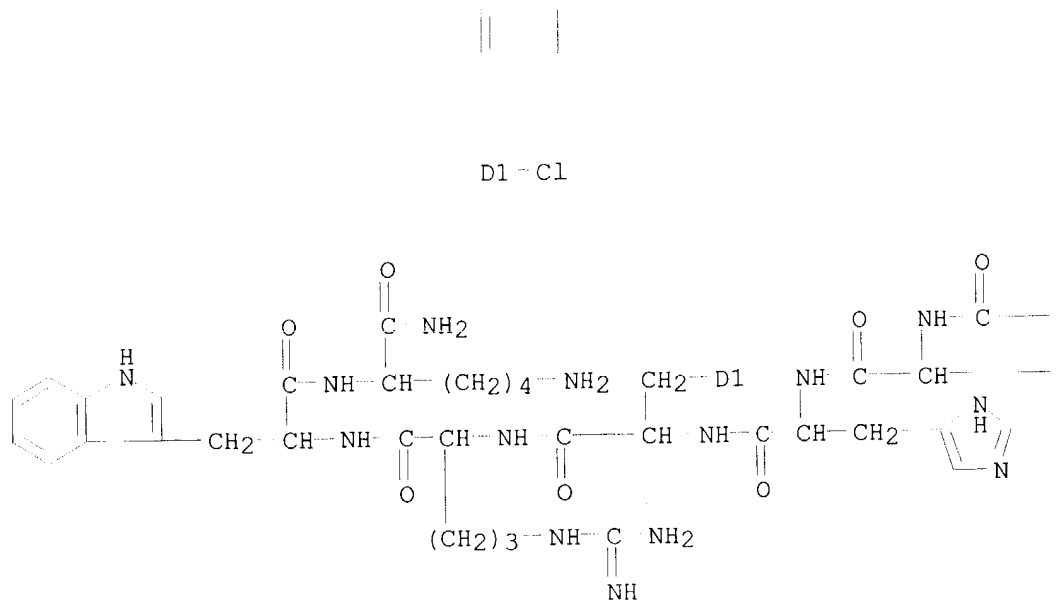
PRIORITY APPLN. INFO.: US 2001-312358P P 20010815

AB The present invention is directed to a group of linear and **cyclic peptides** having the structures: Ac-Nle-Asp-His-D-Phe-Cl-Arg-Trp-Lys-NH2; Ac-Nle-Asp-His-D-Phe-Cl-Arg-Trp-Lys-NH2; Ac-Nle-Asp-His-D-Phe-Cl-Arg-Trp-Lys-Gly-NH2; Ac-Nle-Asp-His-D-Phe-Cl-Arg-Trp-Lys-Gly-Pro-NH2; Ac-Ser-Tyr-Ser-Nle-Asp-His-D-Phe-Cl-Arg-Trp-Lys-NH2; Ac-Tyr-Ser-Nle-Asp-His-D-Phe-Cl-Arg-Trp-Lys-NH2; and Ac-Ser-Nle-Asp-His-D-Phe-Cl-Arg-Trp-Lys-NH2. These peptides, when systemically administered to animals, will bring about a sexual response and are thus useful for the diagnosis and treatment of psychogenic sexual dysfunction in the male.

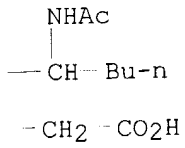
IT **499120-60-4 499120-62-6 499120-64-8**
499120-66-0 499120-68-2 499120-70-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of psychogenic erectile dysfunction)

RN 499120-60-4 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-ar-chloro-D-phenylalanyl-L-arginyl-L-tryptophyl- (9CI) (CA INDEX NAME)

PAGE 1-A



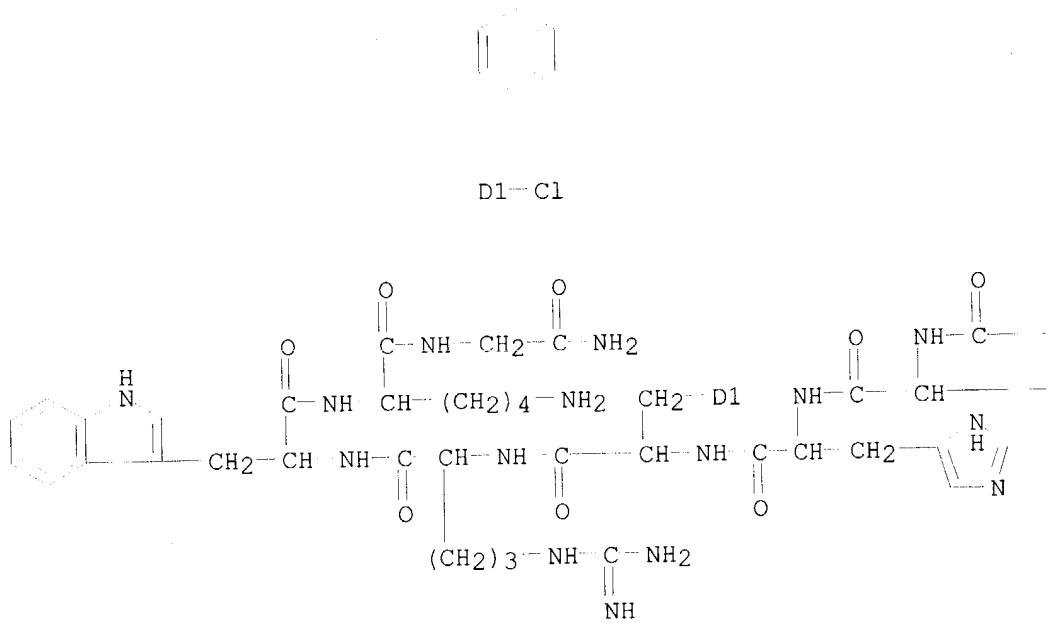
PAGE 1-B



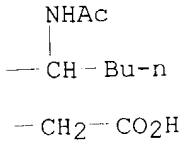
RN 499120-62-6 HCAPLUS
CN Glycinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-ar-chloro-D-phenylalanyl-L-arginyl-L-tryptophyl-L-lysyl- (9CI) (CA INDEX NAME)

Search completed by David Schreiber x22526

PAGE 1-A



PAGE 1-B



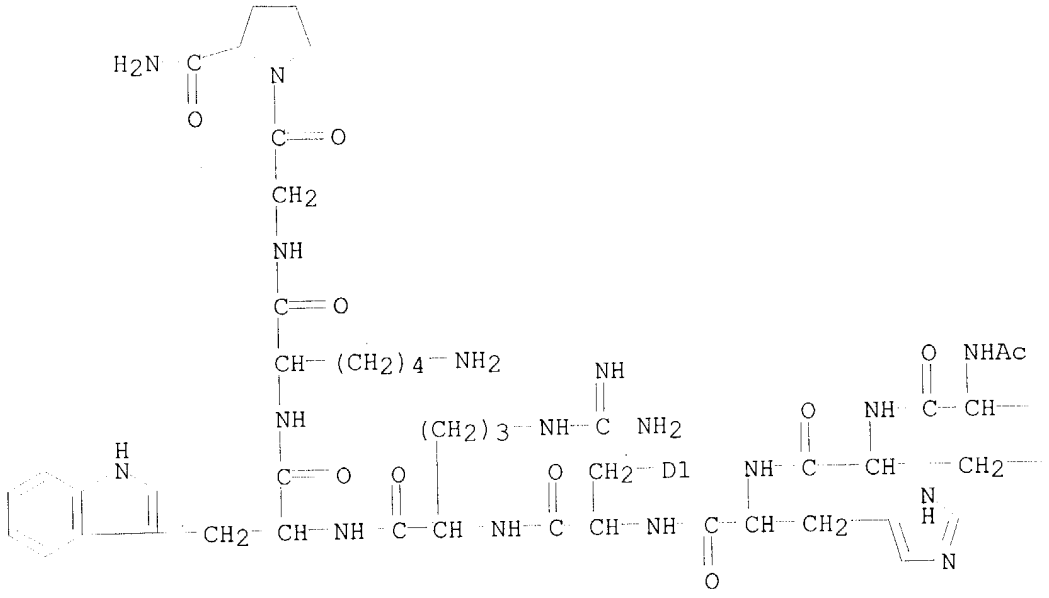
RN 499120-64-8 HCAPLUS
CN L-Prolinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-ar-chloro-D-phenylalanyl-L-arginyl-L-tryptophyl-L-lysylglycyl- (9CI) (CA INDEX NAME)

Search completed by David Schreiber x22526

PAGE 1-A

D1 -- Cl

PAGE 2-A



Search completed by David Schreiber x22526

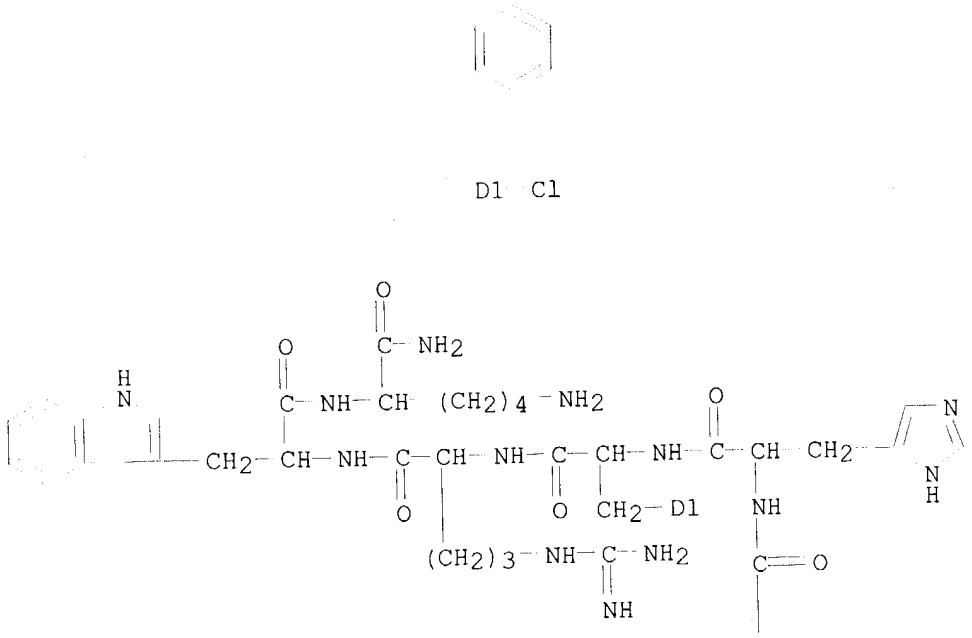
PAGE 2-B

— Bu-n

— CO_2H

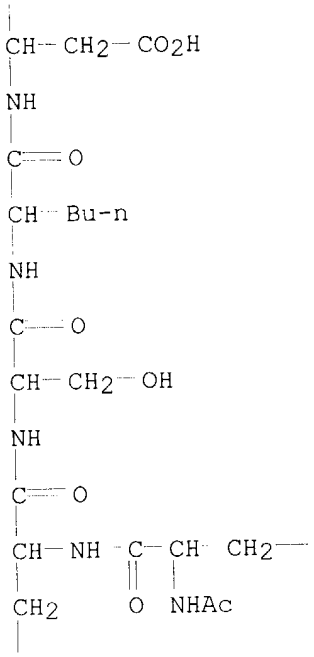
RN 499120-66-0 HCAPLUS
CN L-Lysinamide, N-acetyl-L-seryl-L-tyrosyl-L-seryl-L-norleucyl-L-α-aspartyl-L-histidyl-ar-chloro-D-phenylalanyl-L-arginyl-L-tryptophyl- (9CI) (CA INDEX NAME)

PAGE 1-A



Search completed by David Schreiber x22526

PAGE 2-A



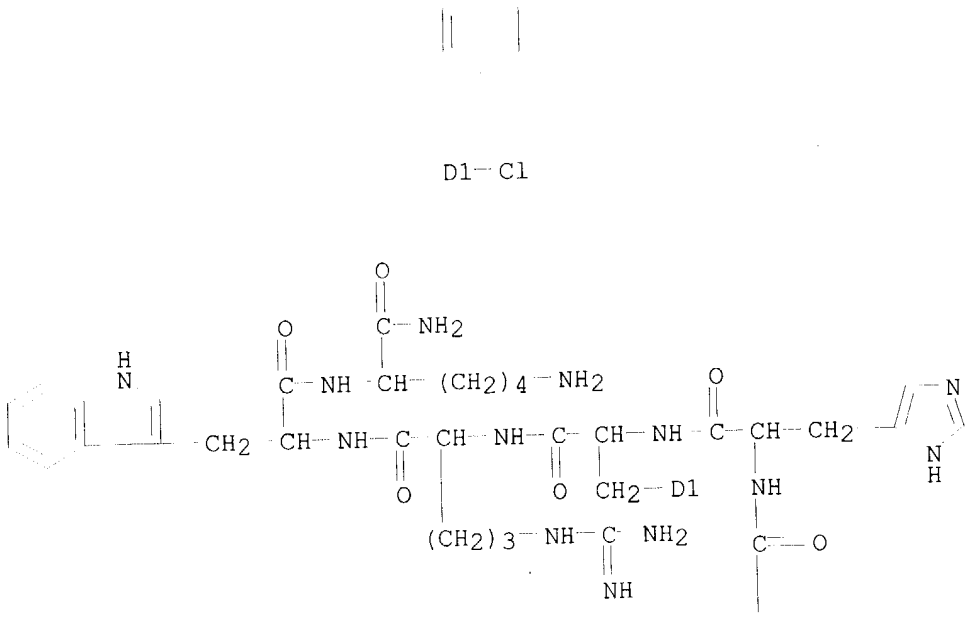
PAGE 2-B

OH

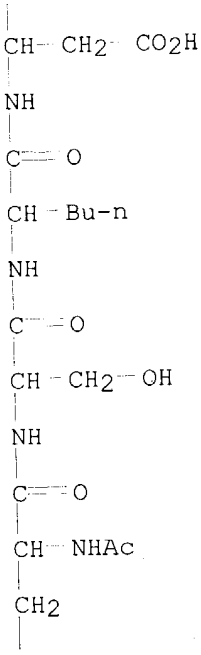
PAGE 3-A

RN 499120-68-2 HCAPLUS
CN L-Lysinamide, N-acetyl-L-tyrosyl-L-seryl-L-norleucyl-L-α-aspartyl-L-histidyl-ar-chloro-D-phenylalanyl-L-arginyl-L-tryptophyl- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



PAGE 3-A

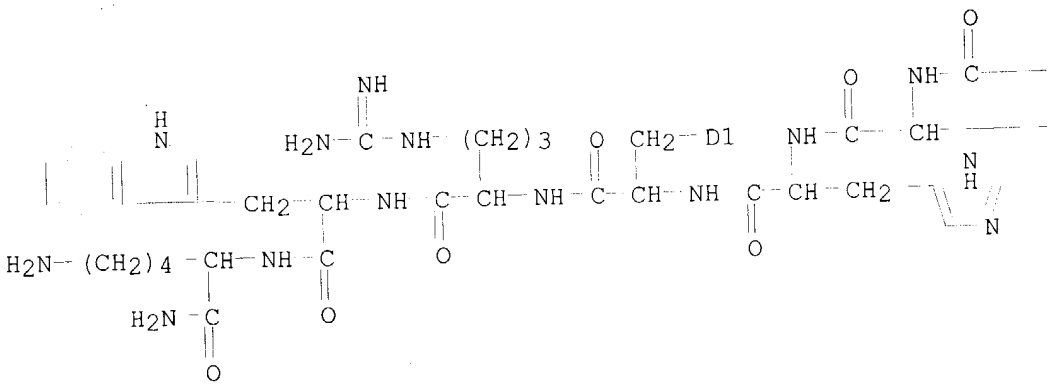
RN 499120-70-6 HCAPLUS
CN L-Lysinamide, N-acetyl-L-seryl-L-norleucyl-L-α-aspartyl-L-histidyl-ar-chloro-D-phenylalanyl-L-arginyl-L-tryptophyl- (9CI) (CA INDEX NAME)

PAGE 1-A

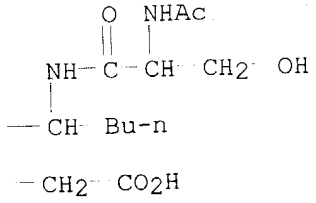
D1- Cl

Search completed by David Schreiber x22526

PAGE 2-A



PAGE 2-B



L15 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:236047 HCAPLUS
DOCUMENT NUMBER: 139:79275
TITLE: Structure-activity relationship of **cyclic peptide** penta-c[Asp-His6-DPhe7-Arg8-Trp9-Lys]-NH2 at the human melanocortin-1 and -4 receptors: His6 substitution
AUTHOR(S): Cheung, Adrian Wai-Hing; Danho, Waleed; Swistok, Joseph; Qi, Lida; Kurylko, Grazyna; Rowan, Karen; Yeon, Mitch; Franco, Lucia; Chu, Xin-Jie; Chen, Li; Yagaloff, Keith
CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ, 07110, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(7), 1307-1311
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

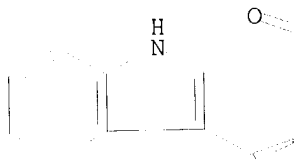
AB A series of MT-II related **cyclic peptides**, based on potent but non-selective hMC4R agonist (Penta-c[Asp-His6-DPhe7-Arg8-Trp9-Lys]-NH2) was prepared in which His6 residue was systematically substituted. Two of the most interesting peptides identified in this study are Penta-c[Asp-5-ClAtc-DPhe-Arg-Trp-Lys]-NH2 and Penta-c[Asp-5-ClAtc-DPhe-Cit-Trp-Lys]-NH2 which are potent hMC4R agonists and are either inactive or weak partial agonists (not tested for their antagonist activities) in hMC1R, hMC3R and hMC5R agonist assays.

Search completed by David Schreiber x22526

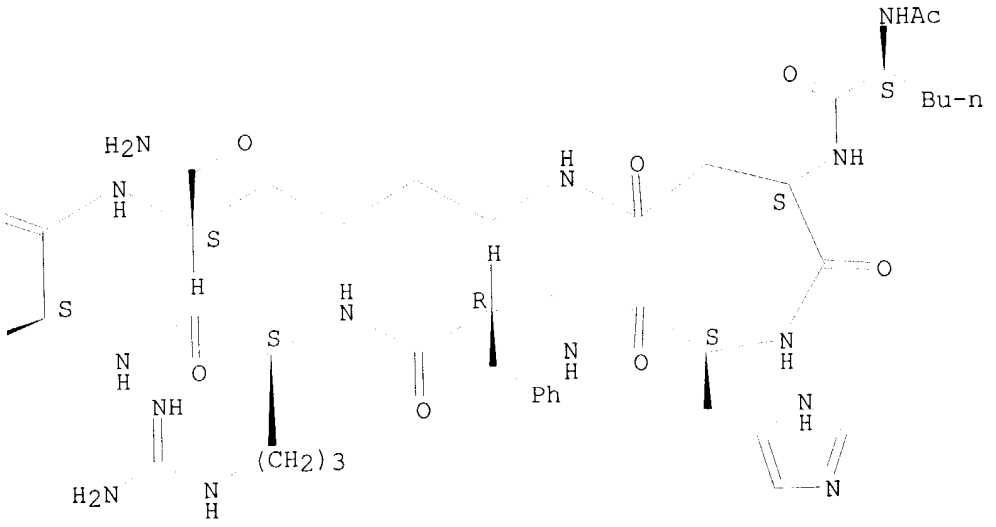
IT **121062-08-6**, MT II
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(structure-activity relationship of His6-substituted **cyclic peptides** penta-c[Asp-His6-DPhe7-Arg8-Trp9-Lys]-NH2 at the human melanocortin-1 and -4 receptors)
RN 121062-08-6 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:223119 HCAPLUS
DOCUMENT NUMBER: 139:47377

Search completed by David Schreiber x22526

TITLE: Molecular determinants of melanocortin 4 receptor ligand binding and MC4/MC3 receptor selectivity
AUTHOR(S): Nickolls, Sarah A.; Cismowski, Mary I.; Wang, Xiaochuan; Wolff, Meira; Conlon, Paul J.; Maki, Richard A.
CORPORATE SOURCE: Neurocrine Biosciences Inc., San Diego, CA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2003), 304(3), 1217-1227
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The mol. basis of ligand recognition by the melanocortin 4 receptor (MC4R) has not been fully defined. In this study, we investigated the mol. determinants of MC4R ligand binding, employing a large array of ligands, using three approaches. First; mol. modeling of the receptor was used to identify Phe284, in transmembrane (TM) 7, as a potential site of ligand interaction. Mutation of Phe284 to alanine reduced binding affinity and potency of peptides containing L-Phe by up to 71-fold but did not appreciably affect binding of linear peptides containing D-Phe, consistent with a hydrophobic interaction between the Phe7 of α-MSH and Phe284. Second, we examined the effect of a naturally occurring mutation in TM3 (I137T) that is linked to obesity. This mutation decreased affinity and potency of **cyclic**, rigid **peptides** but not more flexible peptides, consistent with an indirect effect of the mutation on the tertiary structure of the receptor. Third, we examined the residues that support ligand selectivity for the MC4R over the MC3R. Mutation of Ile125 (TM3) of the MC4R to the equivalent residue of the MC3R (phenylalanine) selectively decreased affinity and potency of MC4R-selective ligands. This effect was mirrored by the reciprocal MC3R mutation F157I. The magnitude of this effect indicates that this locus is not of major importance. However, it is considered that an isoleucine/phenylalanine mutation may affect the orientation of Asp122, which has been identified as a major determinant of ligand binding affinity. Thus, this study provides further characterization of the MC4R binding pocket.

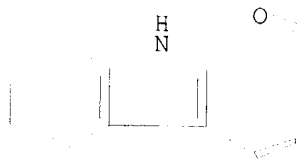
IT **121062-08-6**, MTII **168482-23-3**, SHU9119
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(mol. determinants of melanocortin 4 receptor ligand binding and MC4/MC3 receptor selectivity)

RN 121062-08-6 HCAPLUS

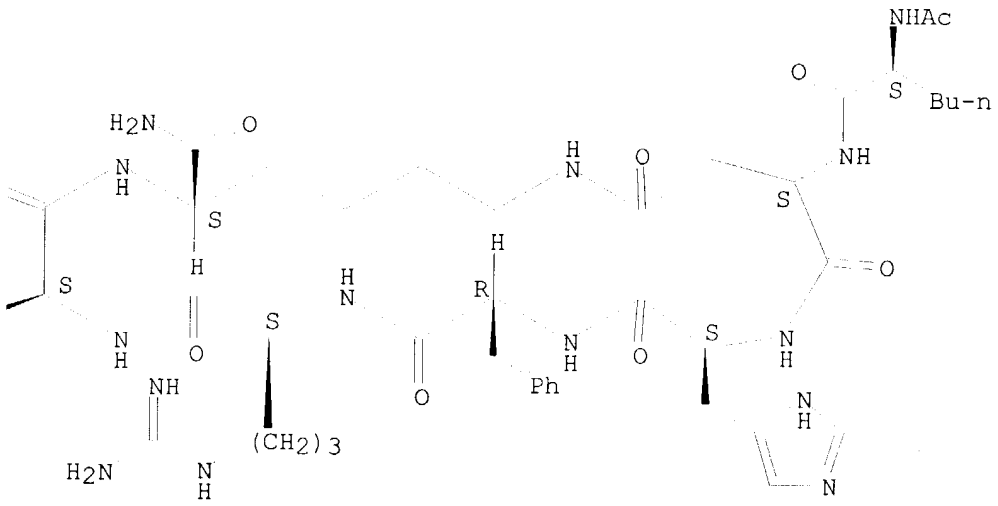
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



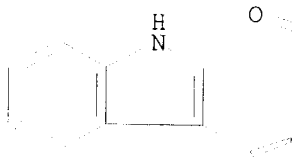
PAGE 1-B



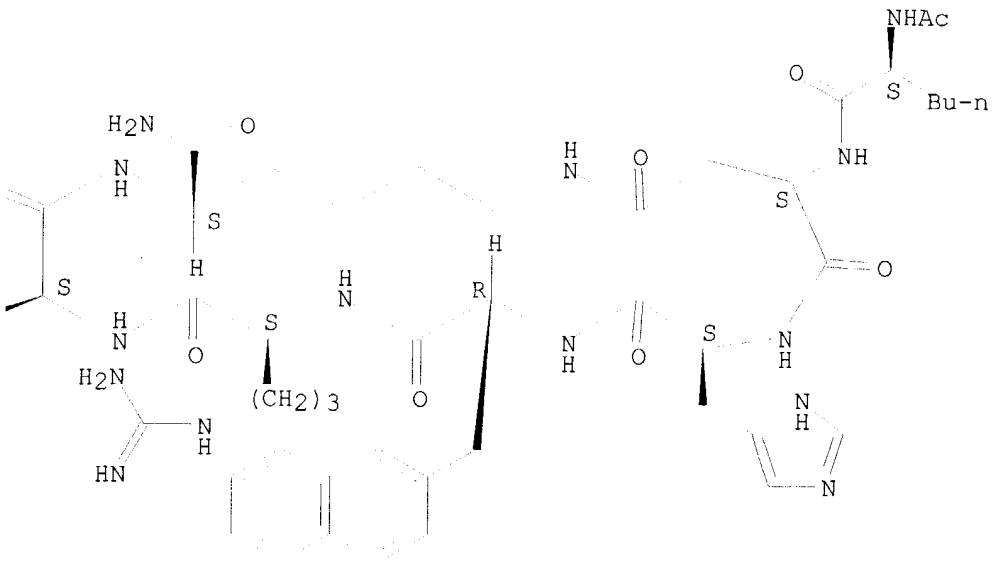
RN 168482-23-3 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-3-(2-naphthalenyl)-D-alanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:83841 HCAPLUS
DOCUMENT NUMBER: 138:379356
TITLE: Novel selective melanocortin 4 receptor antagonist induces food intake after peripheral administration
AUTHOR(S): Schioth, Helgi B.; Kask, Ants; Mutulis, Felikss; Muceniece, Ruta; Mutule, Ilga; Mutule, Ilze; Mandrika, Ilona; Wikberg, Jarl E. S.
CORPORATE SOURCE: Department of Neuroscience, Uppsala University, Uppsala, 751 24, Swed.
SOURCE: Biochemical and Biophysical Research Communications (2003), 301(2), 399-405
CODEN: BBRCA9; ISSN: 0006-291X

Search completed by David Schreiber x22526

PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors synthesized a new series of small cyclic MSH analogs and screened them for binding affinity at the four MSH binding melanocortin (MC) receptors. The authors identified a novel substance HS131, with about 20-fold higher affinity for the MC4 receptor than the MC3 receptor. This substance proved to be antagonist for all the four MC receptors in a cAMP assay. HS131 is a six amino acid long peptide, has a mol. weight below 1000, and has only two amino acids in common with the natural MSH peptides. HS131 potently and dose dependently increased food intake after i.c.v. administration. Moreover, s.c. administration of HS131 (1.0 mg/kg) increased food intake, suggesting that HS131 may be able to pass the blood brain barrier. This **cyclic** low mol. weight **peptidomimetic** will enable studies of the functional role of the MC4 receptors by peripheral administration and it may be used as a template for further development of low mol. weight substances for the MC receptors.

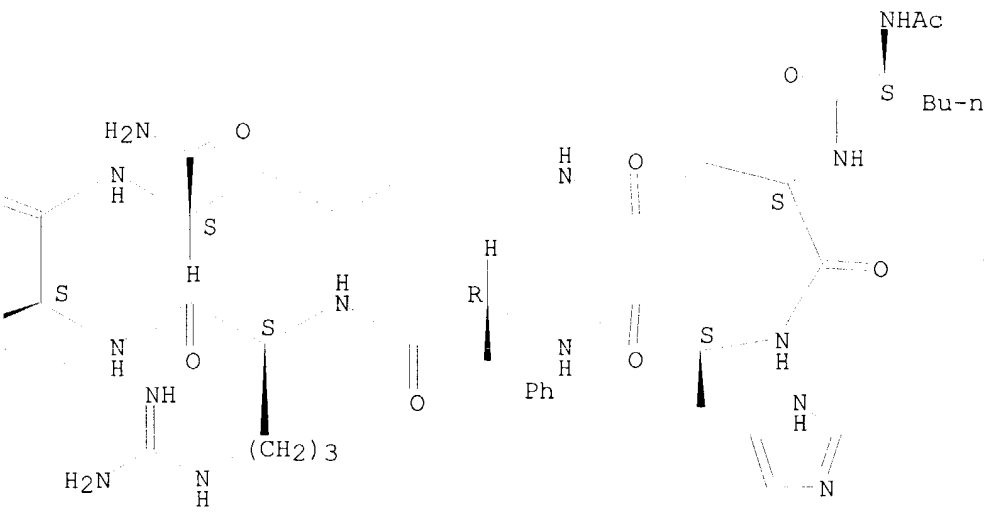
IT **121062-08-6**, MTII **168482-23-3**, SHU9119
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(melanotropin analog binding by melanotropin receptor subtypes and identification of selective melanocortin 4 receptor antagonist inducing food intake after peripheral administration)

RN 121062-08-6 HCAPLUS

CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

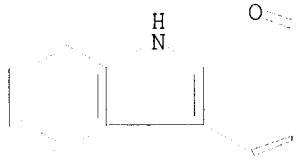
PAGE 1-B



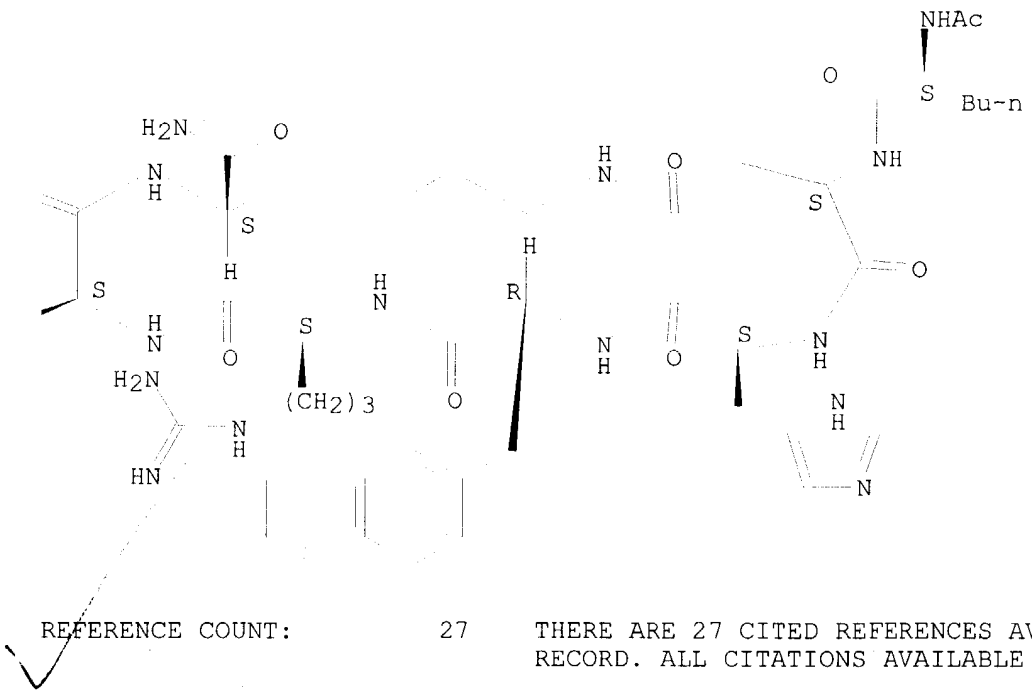
RN 168482-23-3 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-3-(2-naphthalenyl)-D-alanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 28 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 2003319542 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12851303
TITLE: PT-141: a melanocortin agonist for the treatment of sexual dysfunction.
AUTHOR: Molinoff P B; **Shadiack A M**; Earle D; Diamond L E; Quon C Y
CORPORATE SOURCE: Palatin Technologies, Inc, Cranbury, New Jersey 08512, USA.
SOURCE: Annals of the New York Academy of Sciences, (2003 Jun) 994 96-102.
Journal code: 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20030710
Last Updated on STN: 20030830
Entered Medline: 20030829

AB PT-141, a synthetic peptide analogue of alpha-MSH, is an agonist at melanocortin receptors including the MC3R and MC4R, which are expressed primarily in the central nervous system. Administration of PT-141 to rats and nonhuman primates results in penile erections. Systemic administration of PT-141 to rats activates neurons in the hypothalamus as shown by an increase in c-Fos immunoreactivity. Neurons in the same region of the central nervous system take up pseudorabies virus injected into the corpus cavernosum of the rat penis. Administration of PT-141 to normal men and to patients with erectile dysfunction resulted in a rapid dose-dependent increase in erectile activity. The results suggest that PT-141 holds promise as a new treatment for sexual dysfunction.

Search completed by David Schreiber x22526

L15 ANSWER 8 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:595493 HCAPLUS
DOCUMENT NUMBER: 137:145614
TITLE: Pharmaceutical compositions containing a peptide for treatment of sexual dysfunction
INVENTOR(S): Blood, Christine H.; Shadiack, Annette M.; Bernstein, Joanna K.; Herbert, Guy H.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U.S. Ser. No. 606,501.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002107182	A1	20020808	US 2002-40547	20020104
US 6579968	B1	20030617	US 2000-606501	20000628

PRIORITY APPLN. INFO.: US 1999-142346P P 19990629
US 2000-194987P P 20000405
US 2000-606501 A2 20000628

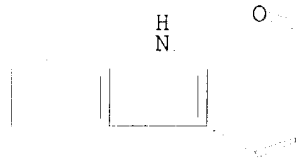
AB Compns. and methods are provided for treatment of sexual dysfunction in mammals, including male sexual dysfunction, such as erectile dysfunction, and female sexual dysfunction. In one embodiment, a peptide-based composition including the peptide sequence Ac-Nle-cyclo(-Asp-His-D-Phe-Arg-Trp-Lys)-OH (I) is administered. Methods of administration include injection, oral, nasal and mucosal administration. I was dissolved in a 50 mM citrate, pH approx. 6.0, at a concentration of .825 mg per mL to obtain a nasal solution Nasal administration of I at a concentration of 25 μk/kg induced 100% penile erection in rats for 2 times in 30 min.

IT **189691-06-3 189691-06-3D**, salts
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing peptide for treatment of sexual dysfunction)

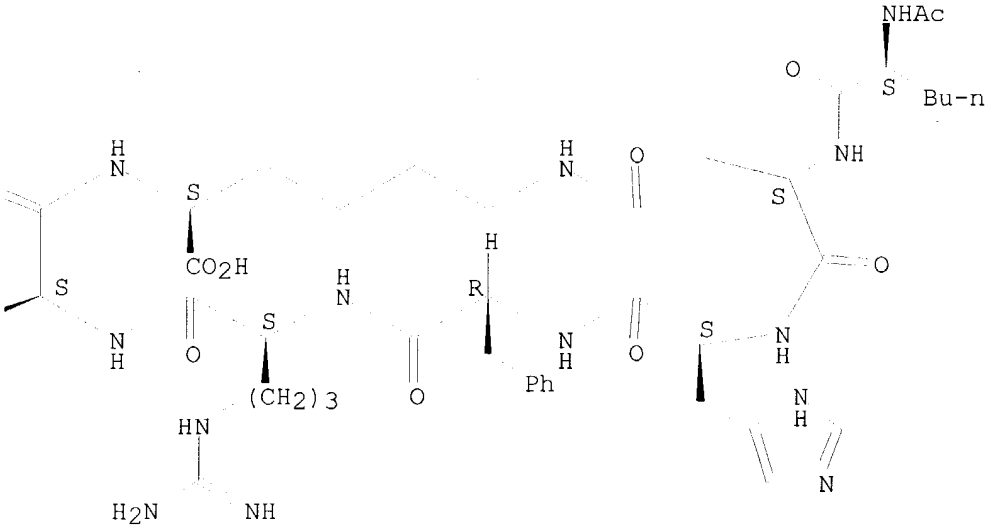
RN 189691-06-3 HCAPLUS
CN L-Lysine, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



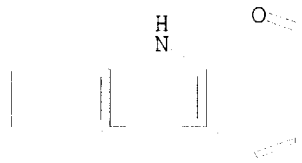
PAGE 1-B



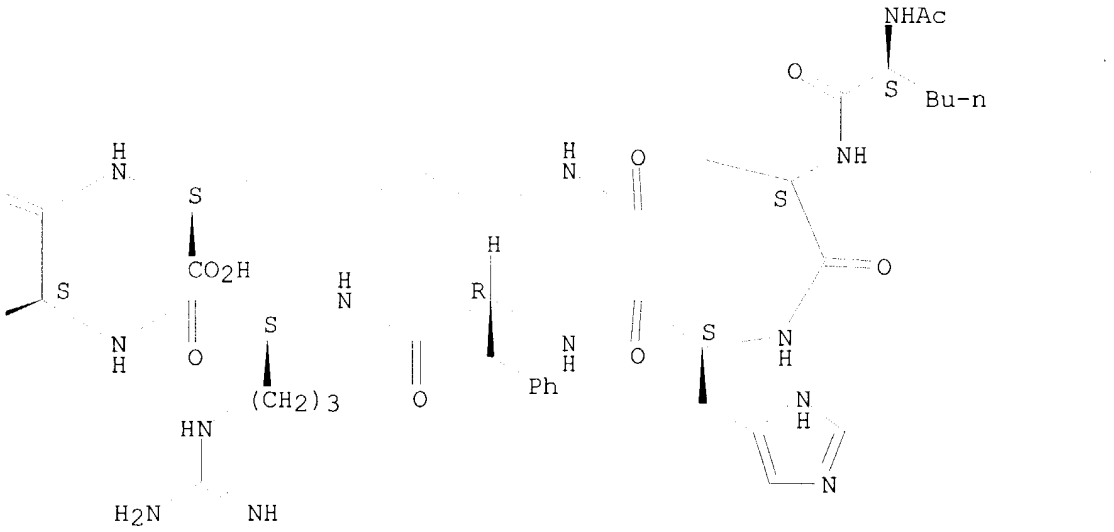
RN 189691-06-3 HCAPLUS
CN L-Lysine, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L15 ANSWER 9 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:171949 HCAPLUS
DOCUMENT NUMBER: 136:217052
TITLE: Preparation of **cyclic peptides** having melanocortin-4 receptor (MC4-R) agonist activity
INVENTOR(S): Chen, Li; Cheung, Adrian Wai-hing; Chu, Xin-jie; Danho, Waleed; Swistok, Joseph; Wang, Yao; Yagaloff, Keith Alan
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 230 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

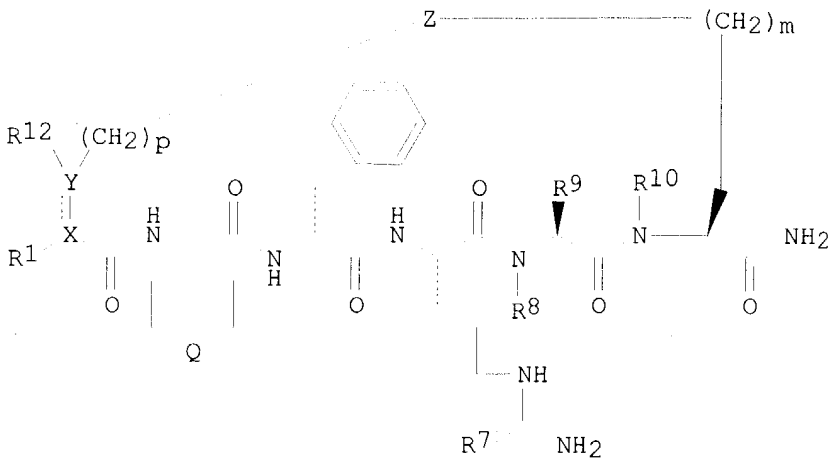
Search completed by David Schreiber x22526

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018437	A2	20020307	WO 2001-EP9630	20010821
WO 2002018437	A3	20020606		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2001084026	A5	20020313	AU 2001-84026	20010821
EP 1315750	A2	20030604	EP 2001-962958	20010821
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004507558	T2	20040311	JP 2002-523951	20010821
US 2002143141	A1	20021003	US 2001-939966	20010827
NO 2003000916	A	20030227	NO 2003-916	20030227

PRIORITY APPLN. INFO.: US 2000-229184P P 20000830
WO 2001-EP9630 W 20010821

OTHER SOURCE(S): MARPAT 136:217052

GI



I

AB The invention refers to peptides I [R1XYR12 is benzo or R1 is H, R2(NH)nCONH (R2 = alkyl, alkenyl, alkynyl; n = 0 or 1), or R2CONHCHR14CONH (R14 is alkyl); R12 is H; XY is C:C or CHCH; Q is (un)substituted methylene or phenylimino; R7 = O, NH; R8, R10 = H, Me; R9 is 3-indenylalkyl, 1- or 2-naphthyl; p = 0 or 1; m = 0-3; Z = CONH or S2], cyclized via disulfide or lactam bridges, having melanocortin-4 receptor (MC4-R) agonist activity and useful for treatment of obesity. Thus, BuCO-cyclo(Asp-Lys)-Asp-Apc-D-Phe-Arg-Trp-Lys-NH2 (Apc = 1-amino-4-phenyl-1-cyclohexanecarboxylic acid residue, Asp-Lys forms a lactam bridge) was prepared by the solid-phase method and showed EC50 = 9.2 and 654 nM, resp., in the MC-4 and MC-1 agonist assays.

IT **121062-08-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

Search completed by David Schreiber x22526

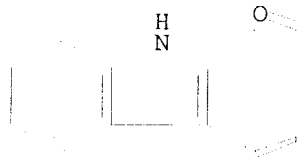
(Uses)
(preparation of **cyclic peptides** having melanocortin-4 receptor (MC4-R) agonist activity)

RN 121062-08-6 HCAPLUS

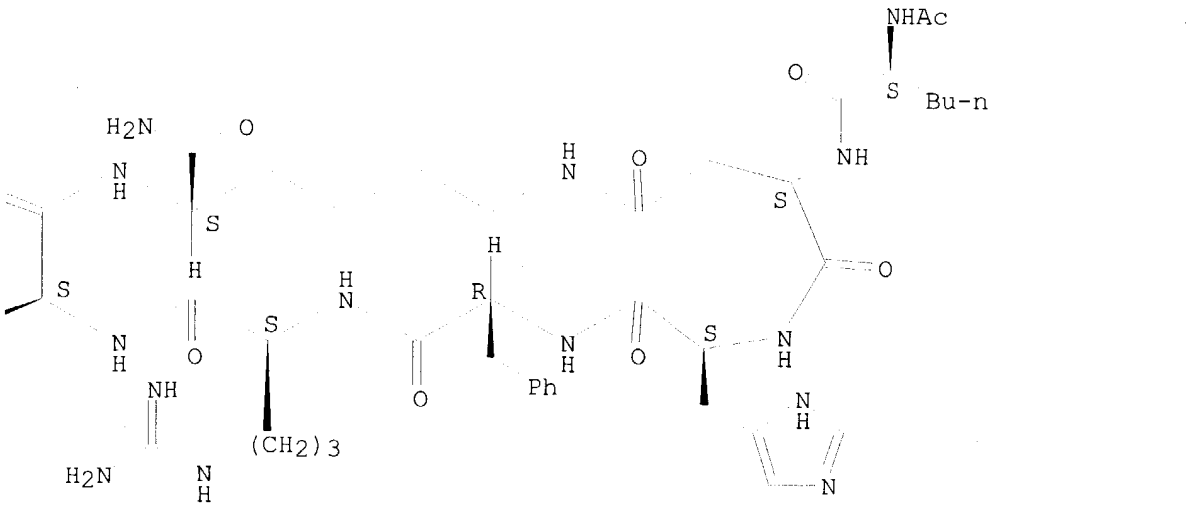
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT **117499-53-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of **cyclic peptides** having melanocortin-4 receptor (MC4-R) agonist activity)

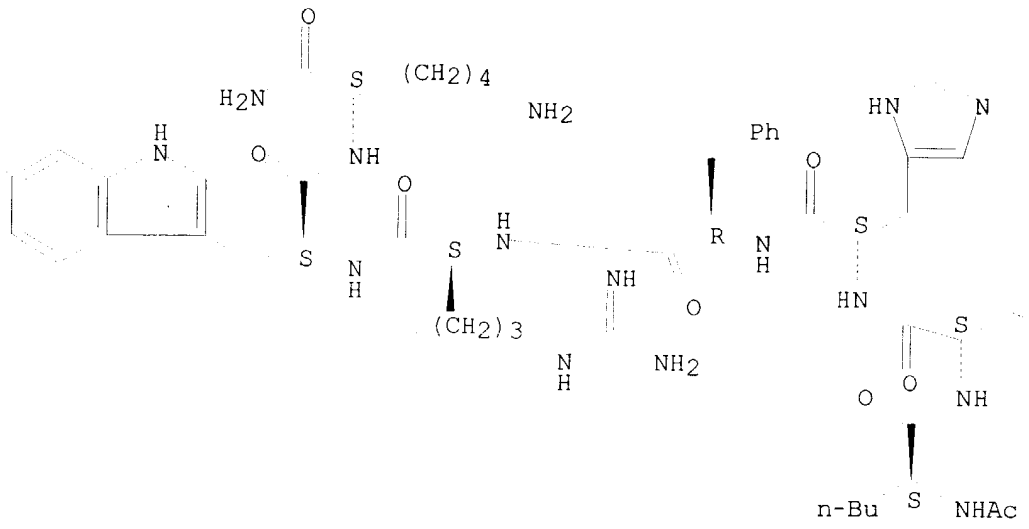
RN 117499-53-3 HCAPLUS

CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl- (9CI) (CA INDEX NAME)

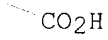
Search completed by David Schreiber x22526

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L15 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2002:808505 HCAPLUS
DOCUMENT NUMBER:	138:19646
TITLE:	Structure-activity studies of the melanocortin peptides: Discovery of potent and selective affinity antagonists for the hMC3 and hMC4 receptors
AUTHOR(S):	Grieco, Paolo; Lavecchia, Antonio; Cai, Minying; Trivedi, Devendra; Weinberg, David; MacNeil, Tanya; Van der Ploeg, L. H. T.; Hruby, Victor J.
CORPORATE SOURCE:	Department of Chemistry, University of Arizona, Tucson, AZ, 85721, USA
SOURCE:	Journal of Medicinal Chemistry (2002), 45(24), 5287-5294 CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER:	American Chemical Society

Search completed by David Schreiber x22526

DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have designed and synthesized several novel cyclic SHU9119 analogs (Ac-Nle4-[Asp5-His6-DNal(2')7-Arg8-Trp9-Lys10]-NH2) modified in position 6 with nonconventional amino acids. SHU9119 is a high affinity nonselective antagonist at hMC3R and hMC4R with potent agonist activity at hMC1R and hMC5R. The authors measured the binding affinity and agonist potency of the novel analogs at cloned hMC3R, hMC4R, and hMC5R receptors and identified several selective, high affinity hMC3R and hMC4R antagonists. Compound 4 containing Che substitution in position 6 is a high affinity hMC4R antagonist (IC50 = 0.48 nM) with 100-fold selectivity over hMC3R antagonist. Analog 7 with a Cpe substitution in position 6 is a high affinity hMC4R antagonist (IC50 = 0.51 nM) with a 200-fold selectivity vs. the hMC3R. Interestingly, analog 9 with an Acpc residue in position 6 is a high affinity hMC3R antagonist (IC50 = 2.5 nM) with 100-fold selectivity vs. the hMC4R antagonist based on its binding affinities. This compound represents the first cyclic lactam antagonist with high selectivity for the hMC3R vs. hMC4R. To understand the possible structural basis responsible for selectivity of these peptides at hMCR3 and hMCR4, the authors have carried out a mol. modeling study to examine the conformational properties of the **cyclic peptides** modified in position 6 with conformationally restricted amino acids.

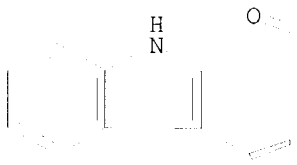
IT **168482-23-3**, SHU9119 **168482-23-3D**, SHU9119, analogs
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(melanocortin peptides binding and antagonist activity at MC3 and MC4 receptors regulation by structure)

RN 168482-23-3 HCAPLUS

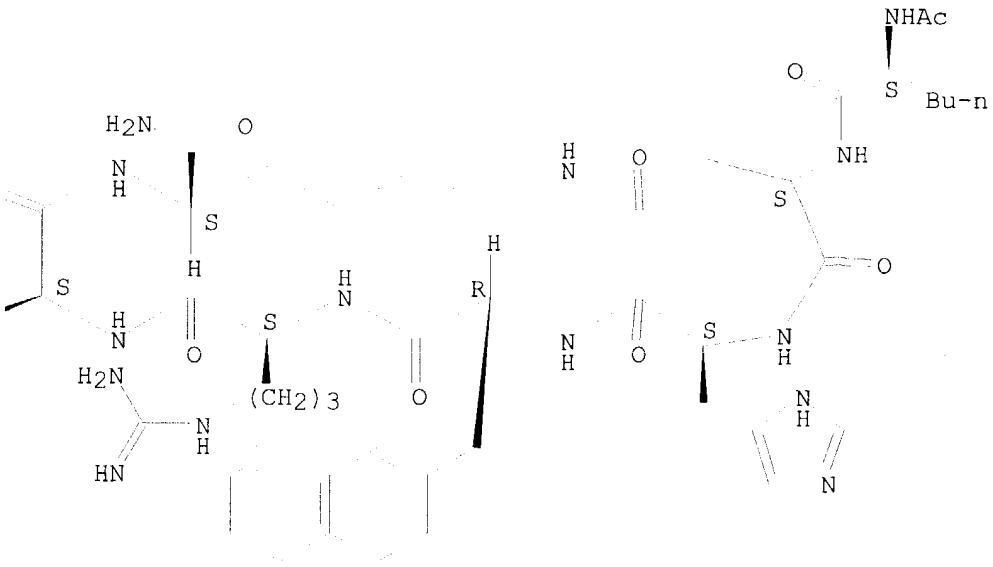
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-3-(2-naphthalenyl)-D-alanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



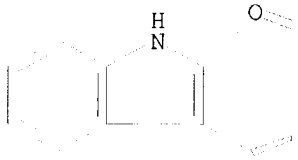
PAGE 1-B



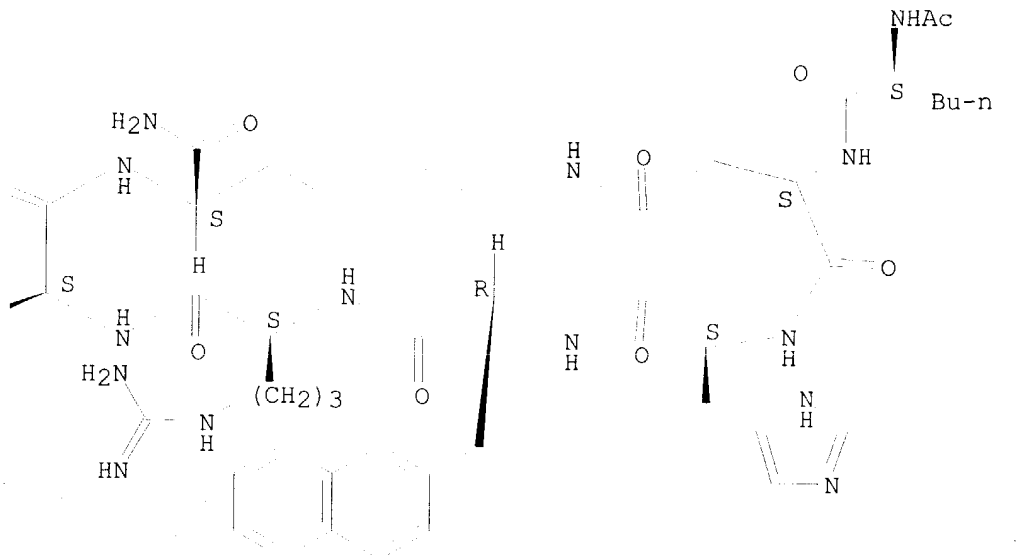
RN 168482-23-3 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-3-(2-naphthalenyl)-D-alanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2001:12284 HCAPLUS
DOCUMENT NUMBER: 134:76409
TITLE: Compositions and methods for treatment of sexual dysfunction
INVENTOR(S): Blood, Christine H.; Shadiack, Annette M.; Bernstein, Joanna K.; Herbert, Guy W.
PATENT ASSIGNEE(S): Palatin Technologies Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000224	A1	20010104	WO 2000-US18217	20000629
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6579968	B1	20030617	US 2000-606501	20000628
BR 2000012200	A	20020326	BR 2000-12200	20000629
EP 1196184	A1	20020417	EP 2000-950283	20000629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

Search completed by David Schreiber x22526

IE, SI, LT, LV, FI, RO
JP 2003503357 T2 20030128 JP 2001-505933 20000629
PRIORITY APPLN. INFO.: US 1999-142346P P 19990629
US 2000-194987P P 20000405
US 2000-606501 A 20000628
WO 2000-US18217 W 20000629

AB Compns. and methods are provided for the treatment of sexual dysfunctions in mammals, such as erectile dysfunction and female sexual dysfunction. In one embodiment, a peptide-based composition including the peptide sequence Ac-Nle-cyclo(-Asp-His-D-Phe-Arg-Trp-Lys)-OH is administered. Methods of administration include injection, oral, nasal and mucosal administration.

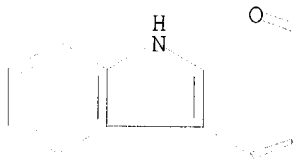
IT **189691-06-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melanocortin analogs for treating sexual dysfunctions)

RN 189691-06-3 HCAPLUS

CN L-Lysine, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

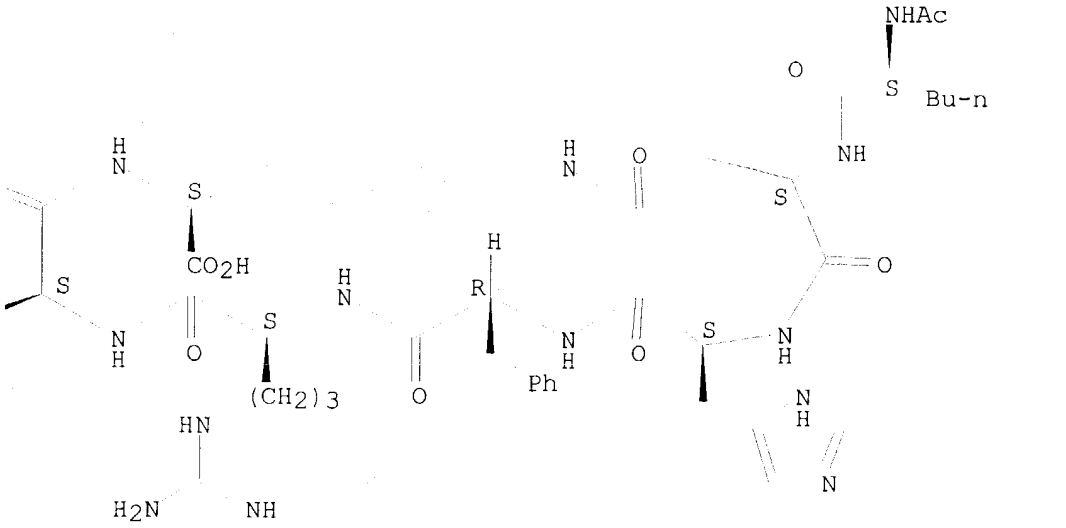
Absolute stereochemistry.

PAGE 1-A



Search completed by David Schreiber x22526

PAGE 1-B



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:719205 HCAPLUS
DOCUMENT NUMBER: 136:32071
TITLE: Selective, high affinity peptide antagonists of α-melanotropin action at human melanocortin receptor 4: Their synthesis and biological evaluation in vitro
AUTHOR(S): Bednarek, Maria A.; MacNeil, Tanya; Kalyani, Rubana N.; Tang, Rui; Van der Ploeg, Lex H. T.; Weinberg, David H.
CORPORATE SOURCE: Departments of Medicinal Chemistry and Obesity Research, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Journal of Medicinal Chemistry (2001), 44(22), 3665-3672
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Peptide Ac-Nle4-cyclo(5β→10ε)(Asp5-His6-D-(2')Nal7-Arg8-Trp9-Lys10)-NH2, compound 1, a cyclic derivative of α-melanotropin, is a nonselective high affinity antagonist at human melanocortin receptors 3 and 4, and an agonist at melanocortin receptors 1 and 5. To differentiate between the physiol. functions of these receptors, antagonists with improved receptor selectivity are needed. In this study, analogs of compound 1 without Ac-Nle4 or His6 and/or the amino group of Asp5 were prepared and tested in binding assays and in functional assays on CHO cells expressing hMC3-5R. Several of these peptides were to be selective, high affinity hMC-4R antagonists. The most interesting was compound 10, named MBP10, cyclo(6β→10ε)(succinyl6-D-(2')Nal7-Arg8-Trp9-Lys10)-NH2, an antagonist (IC50 = 0.5 nM) with 125-fold selectivity over hMC-3R (and of >300-fold selectivity over MC-1RB). This compound had no agonist activity at hMC-3R or hMC-4R and only weak agonist activity at

hMC-5R. Examination of the sequences of these new peptides revealed that the D-(2')Nal7-Arg8-Trp9 segment of peptide 1 forms the "essential core" required for high affinity and high selectivity of analogs of peptide 1 at hMC-4R, but the "extended core", His6-D-(2')Nal7-Arg8-Trp9, is necessary for the maximum affinity for hMC-3R and hMC-5R.

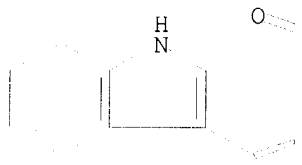
IT **168482-23-3P 215858-99-4P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(selective, high affinity peptide antagonists of α-melanotropin action at human melanocortin receptor 4: synthesis and biol. evaluation in vitro)

RN 168482-23-3 HCAPLUS

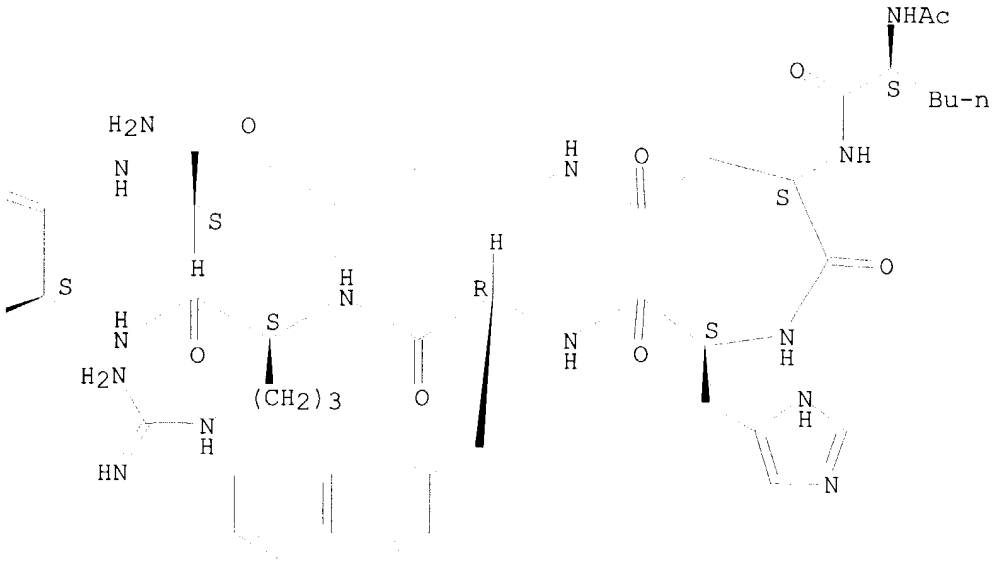
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-3-(2-naphthalenyl)-D-alanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B

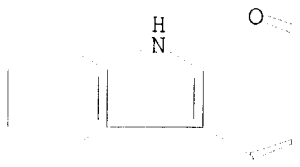


Search completed by David Schreiber x22526

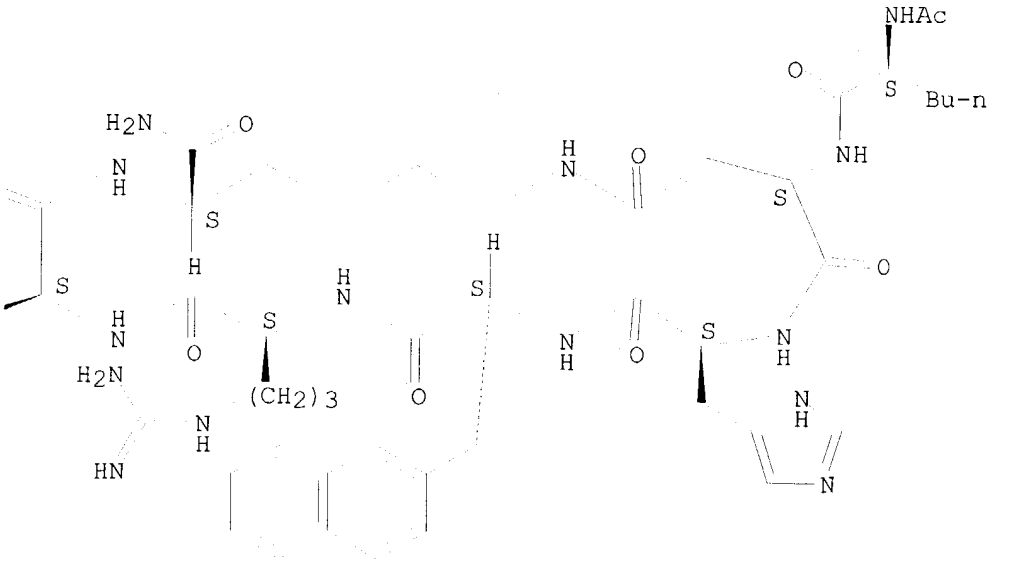
RN 215858-99-4 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-3-(2-naphthalenyl)-L-alanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:692549 HCAPLUS
DOCUMENT NUMBER: 138:313897
TITLE: Highly selective **cyclic peptides** for human melanocortin-4 receptor (MC-4 R): design, synthesis, bioactive conformation, and pharmacological

Search completed by David Schreiber x22526

evaluation as an anti-obesity agent

AUTHOR(S): Danho, Waleed; Swistok, Joseph; Cheung, Adrian; Chu, Xin-Jie; Wang, Yao; Chen, Li; Bartkovitz, David; Gore, Vijay; Qi, Lida; Fry, David; Greeley, David; Sun, Hongmao; Guenot, Jeanmarie; Franco, Lucia; Kurylko, Grazyna; Rumennik, Leonid; Yagaloff, Keith

CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ, 07110, USA

SOURCE: Peptides: The Wave of the Future, Proceedings of the Second International and the Seventeenth American Peptide Symposium, San Diego, CA, United States, June 9-14, 2001 (2001), 701-703. Editor(s): Lebl, Michal; Houghten, Richard A. American Peptide Society: San Diego, Calif.
CODEN: 69DBAL; ISBN: 0-9715560-0-8

DOCUMENT TYPE: Conference

LANGUAGE: English

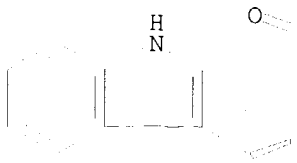
AB The use of a selective melanocortin receptor-4 (MCR-4) **cyclic peptide** agonist as a pharmacol. tool in obesity and feeding studies was evaluated, and a pharmacophore model applicable to structure-based drug design was developed. Each of the four core amino acids of the MTII MCR-4 agonist was systematically replaced with conformationally constrained amino acids to evaluate the analogs in binding and cAMP assay at the human MC-1, -3, -4, and -5 receptors. The amino acid position occupied by His is the most critical position responsible for the selectivity of MC-4 against the other MC-receptors. A correlation was noted between high potency and the presence of a β turn at position corresponding to Asp-His-(D)Phe-Arg in the parent sequence.

IT **121062-08-6**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(design, synthesis and bioactive conformation of highly selective peptides for human melanocortin-4 receptor and pharmacol. evaluation as anti-obesity agents)

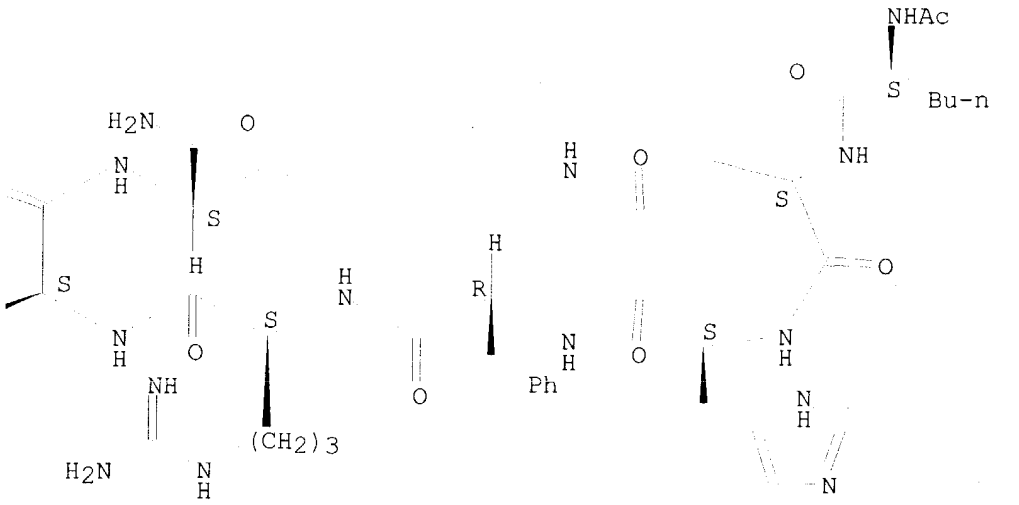
RN 121062-08-6 HCAPLUS

CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:509678 HCAPLUS
DOCUMENT NUMBER: 140:175300
TITLE: Synthesis and conformational studies of **cyclic peptides** with antagonist activity at melanocortin 3 and 4 receptors
AUTHOR(S): Grieco, Paolo; Novellino, Ettore; Lavecchia, Antonio; Weinberg, David; MacNeil, Tanya; Hruby, Victor J.
CORPORATE SOURCE: Dept. of Chemistry, University of Arizona, Tucson, AZ, USA
SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 643-644. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr.
CODEN: 69EDWK; ISBN: 2-84254-048-4
DOCUMENT TYPE: Conference
LANGUAGE: English

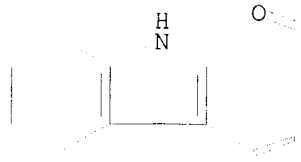
AB Analogs of SHU9119 (Ac-Nle-[Asp-His-DNal-Arg-Trp-Lys]-NH2), i.e., peptides PG-913, PG-914, and PG-915, were synthesized in which His6 residue was replaced by the unconventional amino acids Oic, Che and Aic, resp. The compound PG-913 was more selective toward the melanocortin 3 receptor (MC3R), whereas PG-915 had selectivity on the MC4R. Mol. modeling studies showed that the selectivity for MC3R over MC4R depends on steric properties of the residue in position 6 rather than on different overall conformational behavior.

IT **168482-23-3**, SHU9119
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(synthesis and conformational studies of **cyclic peptides** with antagonist activity at melanocortin 3 and 4 receptors)
RN 168482-23-3 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-3-(2-

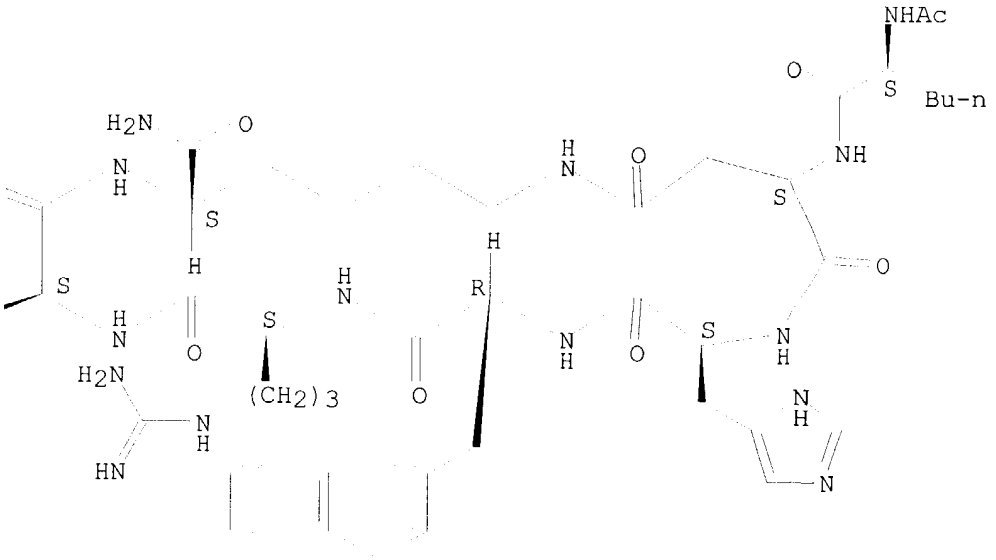
naphthalenyl)-D-alanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 15 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:707211 HCAPLUS
DOCUMENT NUMBER: 133:267160
TITLE: Preparation of **cyclic peptides** as melanocortin receptor ligands
INVENTOR(S): Mazur, Adam Wieslaw; Wang, Feng; Sheldon, Russell James; Ebetino, Frank Hal
PATENT ASSIGNEE(S): The Procter & Gamble Company, USA
SOURCE: PCT Int. Appl., 66 pp.

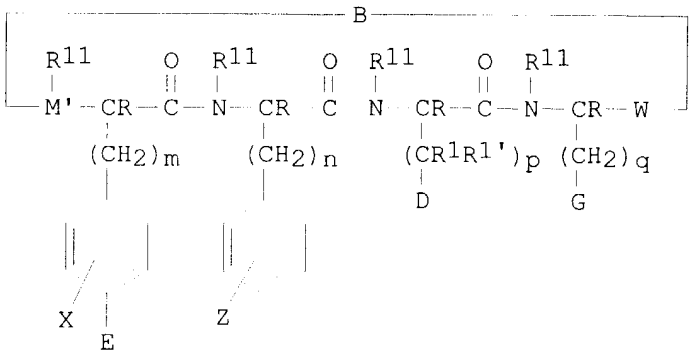
Search completed by David Schreiber x22526

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058361	A1	20001005	WO 2000-US7473	20000321
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
NZ 514141	A	20010928	NZ 2000-514141	20000321
EP 1165613	A1	20020102	EP 2000-919500	20000321
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000009497	A	20020115	BR 2000-9497	20000321
TR 200102765	T2	20020521	TR 2001-20010276520000321	
JP 2002542159	T2	20021210	JP 2000-608653	20000321
AU 763510	B2	20030724	AU 2000-40179	20000321
AU 2000040179	A5	20001016		
RU 2213098	C2	20030927	RU 2001-128890	20000321
US 6613874	B1	20030902	US 2000-537789	20000329
ZA 2001007411	A	20020312	ZA 2001-7411	20010907
NO 2001004568	A	20011129	NO 2001-4568	20010920
US 2004023859	A1	20040205	US 2003-612104	20030702

PRIORITY APPLN. INFO.:
US 1999-126673P P 19990329
WO 2000-US7473 W 20000321
US 2000-537789 A1 20000329

OTHER SOURCE(S): MARPAT 133:267160
GI



I

AB **Cyclic peptide** analogs I [m, n, q = 0-4; p = 0-5; X, E, Z = H, halo, OH, SH, NH2, alkyl, cyano, nitro,aryl, heteroaryl, etc.; D = (un)substituted guanidino; R1, R1' = H, alkyl, aryl, heteroaryl or CR1R1' = cycloalkyl or aryl; G = optionally substituted bicyclic aryl or

heteroaryl; R, R11 = H, alkyl, alkene, alkyne, aryl, heteroaryl, cycloalkyl or R and R11 may join together to form a ring; W = covalent bond, CH2, CO; M' = N, CH; B is an optionally substituted bridge moiety that links M' and W to form a ring and comprises a covalent bond or a ionic bond which may be substituted by ≤ 3 amino acid residues] were prepared for use in treating diseases that are mediated by the melanocortin (MC)-4 and/or the MC-3 receptor. Thus, Ac-a[DYfRWGK]-NH2 (brackets denote amino acid points of cyclization) was prepared by the solid-phase method and evaluated for melanocortin functional activity and selectivity.

IT **117499-53-3P 213314-49-9P**

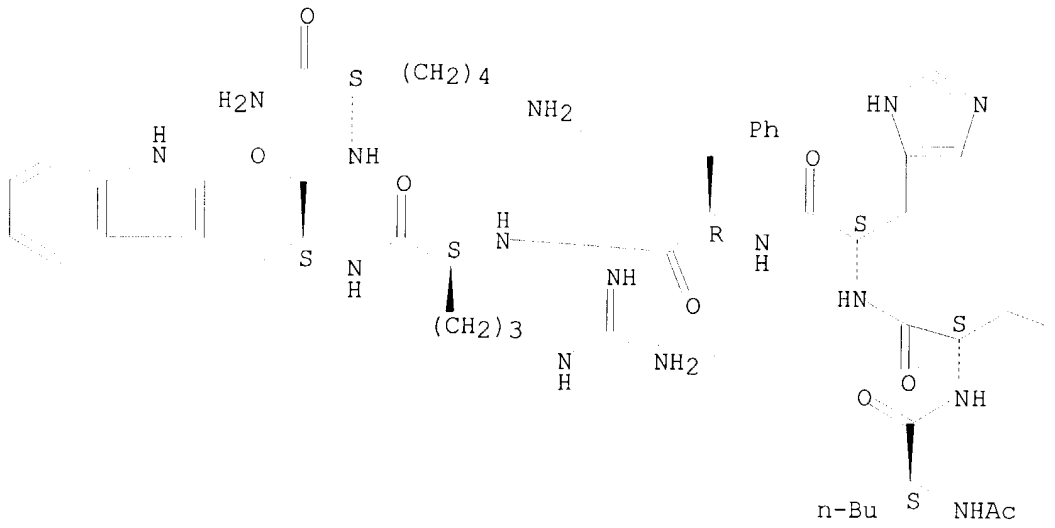
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **cyclic peptides** as melanocortin receptor ligands)

RN 117499-53-3 HCAPLUS

CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



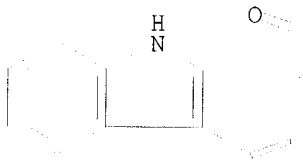
PAGE 1-B

CO_2H

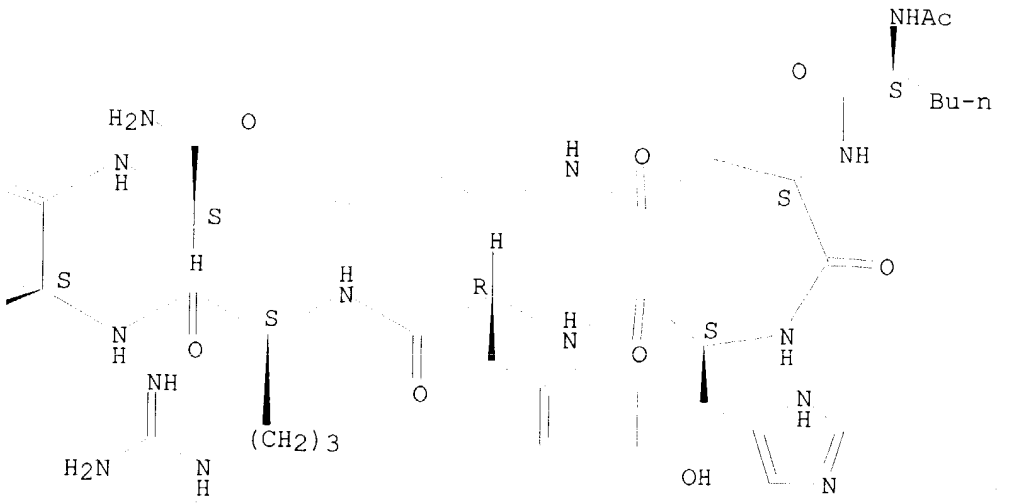
RN 213314-49-9 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-tyrosyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:401591 HCAPLUS
DOCUMENT NUMBER: 133:38707
TITLE: Composition and method for regulation of body weight and associated conditions by administering proopiomelanocortin peptides or analogs thereof
INVENTOR(S): Brennan, Miles B.; Hochgeschwender, Ute
PATENT ASSIGNEE(S): Eleanor Roosevelt Institute, USA; Oklahoma Medical Research Foundation
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000033658	A1	20000615	WO 1999-US29337	19991209
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6603058	B1	20030805	US 1999-374827	19990812
EP 1137340	A1	20011004	EP 1999-965208	19991209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2003144174	A1	20030731	US 1999-458579	19991209

Search completed by David Schreiber x22526

US 6716810 B1 20040406 US 1999-458580 19991209
PRIORITY APPLN. INFO.: US 1998-111581P P 19981209
US 1999-146299P P 19990729
US 1999-146300P P 19990729
US 1999-146301P P 19990729
US 1999-146302P P 19990729
US 1999-146303P P 19990729
US 1999-146304P P 19990729
US 1999-146305P P 19990729
US 1999-146306P P 19990729
US 1999-374827 A 19990812
WO 1999-US29337 W 19991209

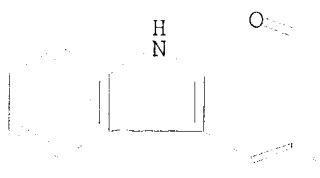
OTHER SOURCE(S): MARPAT 133:38707

AB Described are methods and compns. for regulating body weight and/or regulating the rate of weight gain or loss, and particularly, for treating or preventing obesity. Specifically, methods of administering varying levels of **circulating** proopiomelanocortin **peptides** or analogs thereof to an animal, alone or in combination with leptin or other body weight regulating agents are disclosed. Methods and compns. for treating a variety of disorders associated with or caused by undesirable body weight are also described. Also described are methods for identifying compds. useful for regulation of body weight and associated conditions. In particular, methods are disclosed for identification of compds. that preferentially bind to and/or activate peripheral melanocortin receptors and which minimize binding and/or activation of central melanocortin receptors. Also described is a genetically modified non-human animal model for studying the peripheral and central pathways of energy homeostasis. Also disclosed are methods of identifying compds. for regulating such pathways and a POMC mutant mouse. The compns. of the invention include food and pharmaceutical compns.

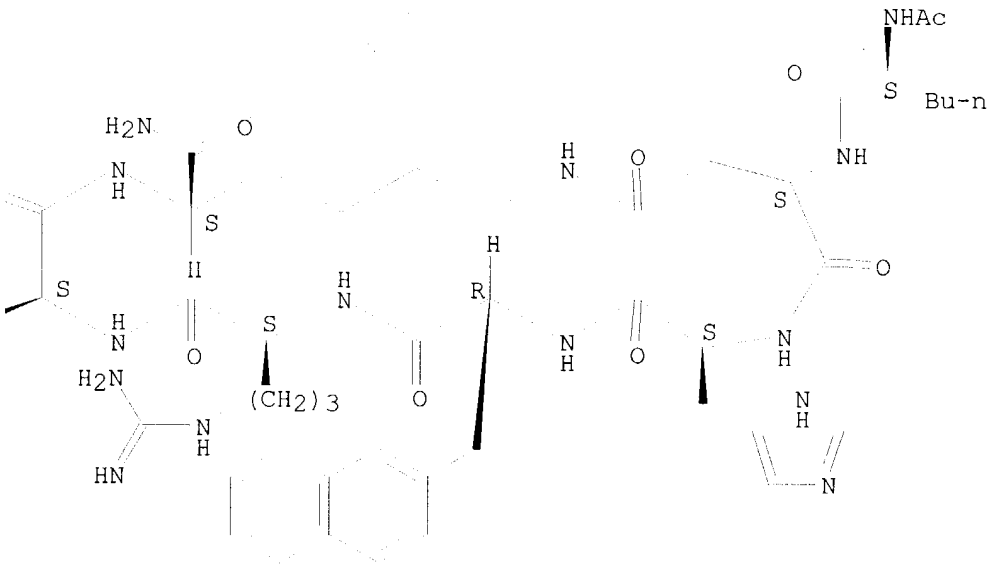
IT **168482-23-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition and method for regulation of body weight and associated conditions by administering proopiomelanocortin peptides or analogs thereof)

RN 168482-23-3 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-3-(2-naphthalenyl)-D-alanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



PAGE 1-B



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 17 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:508309 HCAPLUS
DOCUMENT NUMBER: 131:252673
TITLE: Structure-function studies on the **cyclic peptide** MT-II, lactam derivative of α-melanotropin
AUTHOR(S): Bednarek, Maria A.; Silva, Maria V.; Arison, Byron; MacNeil, Tanya; Kalyani, Rubana N.; Huang, Ruey-Ruey C.; Weinberg, David H.
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Peptides (New York) (1999), 20(3), 401-409
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The alanine-substituted and the retro, enantio, and retro-enantio analogs of MT-II, a potent agonist at melanocortin (MC) receptors, were prepared by solid-phase synthesis and evaluated for their ability to bind and activate human MC3, MC4, and MC5 receptors. Replacement of His with Ala resulted in [Ala6]-MT-II with affinity and agonist potency at human MC3, MC4, and MC5 receptors similar to MT-II. Substitution of Arg with Ala gave compound 100-fold less potent than MT-II, but replacement of Phe of Trp with Ala led to inactive compds. (at the micromolar concns.). The significant drop of potency of the retro, enantio, and retro-enantio analogs of MT-II, demonstrated a crucial role of side-chain topol., and to a lesser degree, of peptide backbone in interactions of MT-II with the melanocortin receptors. The NMR anal. of MT-II suggested involvement of Phe and Arg

residues in H-bonds stabilizing the bent conformations of the peptide backbone.

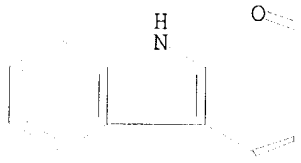
IT **121062-08-6**, MT-II **168482-23-3**, SHU9119
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(structure-function studies on **cyclic peptide** MT-II, lactam derivative of α-melanotropin)

RN 121062-08-6 HCAPLUS

CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

RN 168482-23-3 HCAPLUS

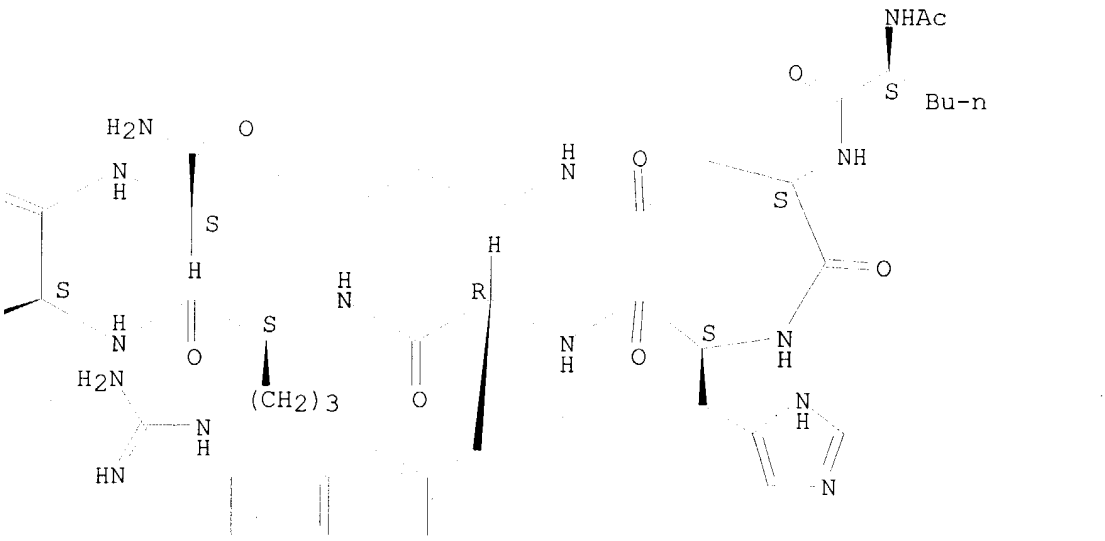
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-3-(2-naphthalenyl)-D-alanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Search completed by David Schreiber x22526

Absolute stereochemistry. Rotation (-).

PAGE 1-A

PAGE 1-B



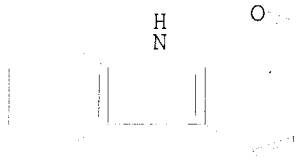
IT **245040-71-5P 245040-74-8P 245040-77-1P**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(structure-function studies on **cyclic peptide** MT-II, lactam derivative of α-melanotropin)

RN 245040-71-5 HCAPLUS

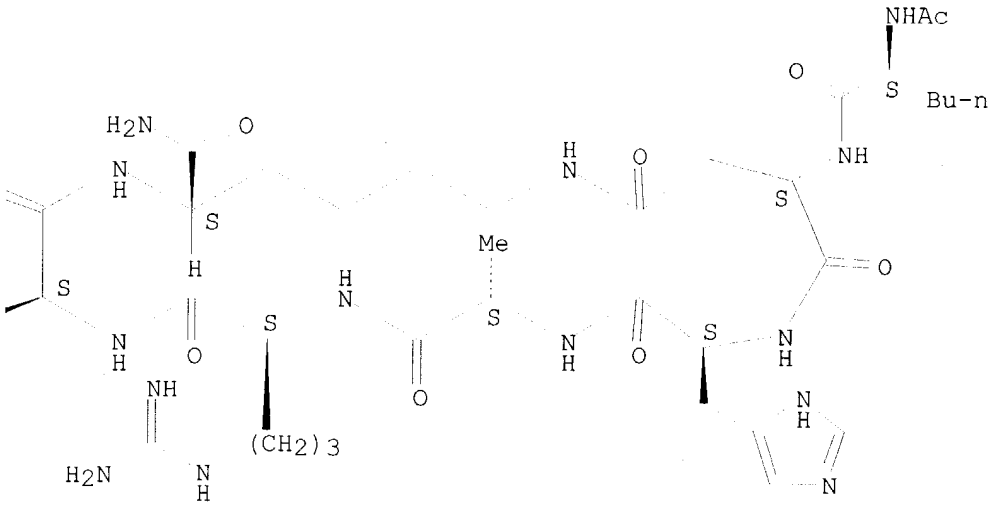
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-L-alanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



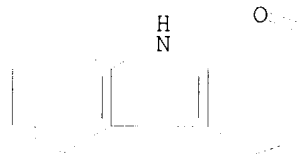
PAGE 1-B



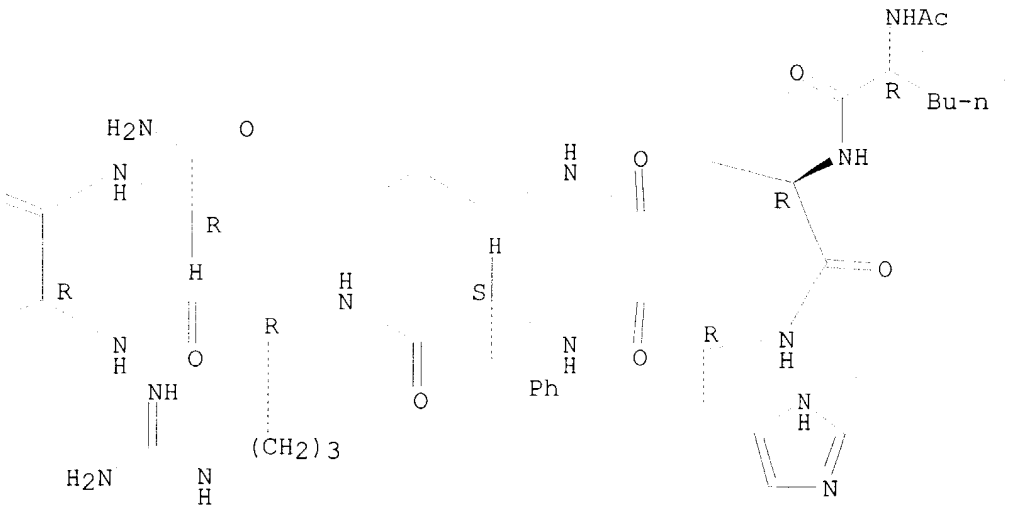
RN 245040-74-8 HCAPLUS
CN D-Lysinamide, N-acetyl-D-norleucyl-D-α-aspartyl-D-histidyl-L-phenylalanyl-D-arginyl-D-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

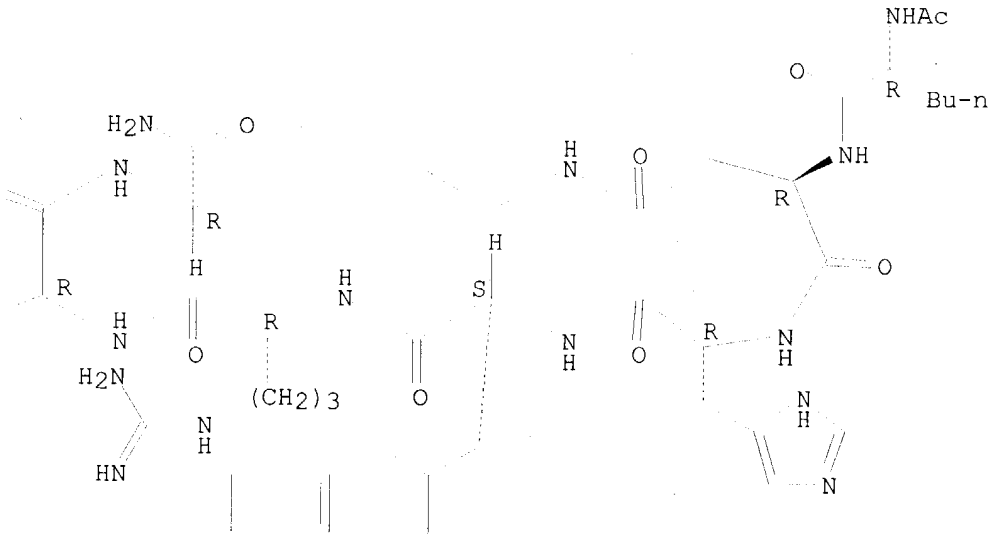


RN 245040-77-1 HCAPLUS
CN D-Lysinamide, N-acetyl-D-norleucyl-D-α-aspartyl-D-histidyl-3-(2-naphthalenyl)-L-alanyl-D-arginyl-D-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:192146 HCAPLUS
DOCUMENT NUMBER: 128:257693
TITLE: Preparation of peptides having potent antagonist and agonist bioactivities at melanocortin receptors
INVENTOR(S): Hadley, Mac E.; Hruby, Victor J.; Sharma, Shubh D.
PATENT ASSIGNEE(S): University of Arizona, Board of Regents, USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

Search completed by David Schreiber x22526

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5731408	A	19980324	US 1995-420972	19950410
US 6054556	A	20000425	US 1997-980238	19971128

PRIORITY APPLN. INFO.: US 1995-420972 19950410

GI

Ac-Nle-Asp-His-X-Arg-Trp-Lys-NH_2 I

AB **Cyclic** lactam **peptides** I [X = D-3-(2-naphthyl)alanine (D-2-Nal), D-p-iodophenylalanine [D-(p-I)Phe]] provided potent and specific antagonists of the two neural melanocortin receptors and of the peripheral receptor. In particular, peptide I (X = D-2-Nal) was a potent antagonist of the MC3 and MC4 receptors with partial agonist activity, and a full agonist of the MC1 and MC5 receptors. Peptide I [X = D-(p-I)Phe] was a potent antagonist of the MC3 and MC4 receptors with partial agonist activity. Both peptides I have antagonist activities in the classical frog skin bioassay for pigmentation at the MC1 receptor.

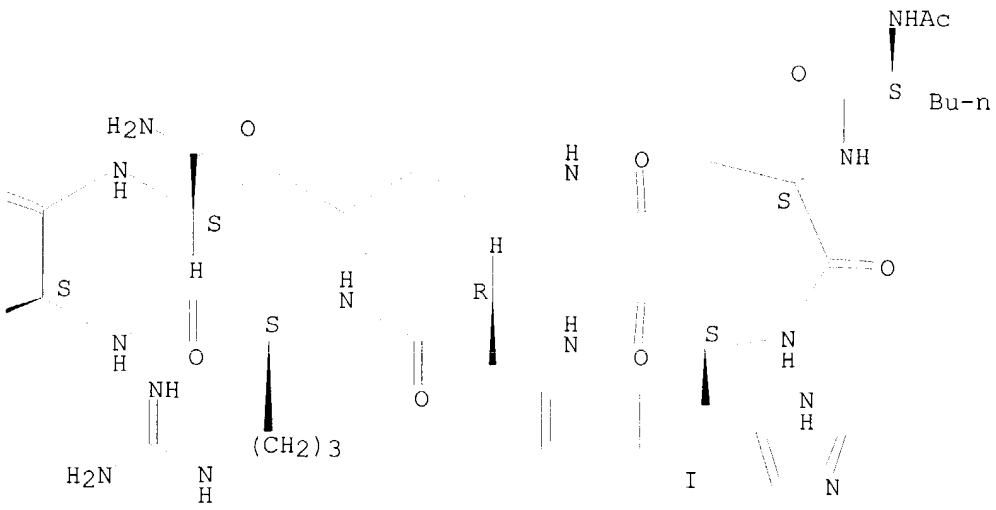
IT **168482-22-2P 168482-23-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of peptides having potent antagonist and agonist bioactivities at melanocortin receptors)

RN 168482-22-2 HCAPLUS

CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-4-iodo-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-B

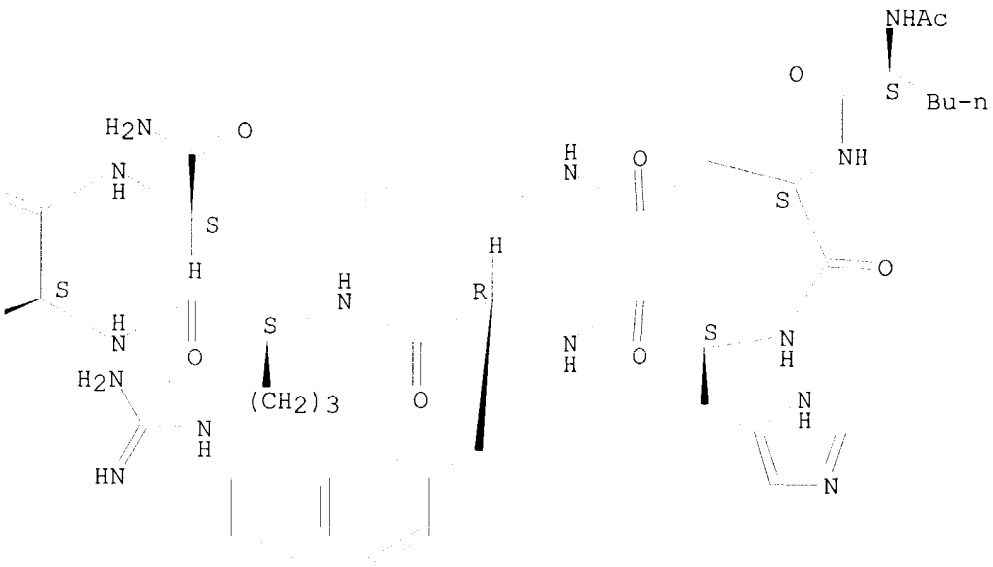


RN 168482-23-3 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-3-(2-naphthalenyl)-D-alanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A

PAGE 1-B



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:388818 HCAPLUS
DOCUMENT NUMBER: 131:19304
TITLE: Linear and cyclic analogs of alpha-MSH fragments with extraordinary potency
INVENTOR(S): Hruby, Victor J.; Al-Obeidi, Fahad A.; Hadley, Mac E.
PATENT ASSIGNEE(S): University Patents, Inc., USA
SOURCE: Can., 42 pp.
CODEN: CAXXA4
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 1340107	A1	19981027	CA 1988-578920	19880930

PRIORITY APPLN. INFO.: CA 1988-578920 19880930

AB Cyclic alpha-MSH analogs are claimed for the manufacture of medicaments having melanotropic activity. Thus, Ac-[Nle4,D-Phe7,Lys10,Gly11]-alpha-MSH4-13NH2 was prepared by the solid-phase method. This linear peptide and its cyclized form showed prolonged melanocyte-stimulating activity in frog and lizard assays.

IT **117499-48-6P 117499-53-3P 117603-87-9P**
121062-05-3P 121062-08-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of linear and cyclic analogs of alpha-MSH fragments with extraordinary potency)

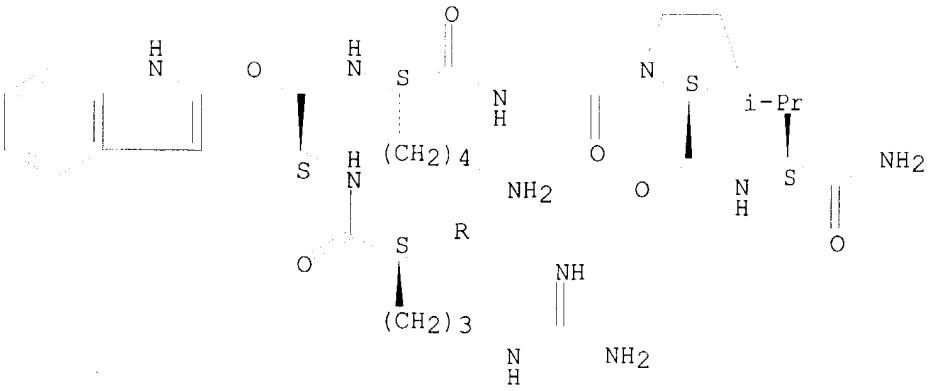
RN 117499-48-6 HCAPLUS

Search completed by David Schreiber x22526

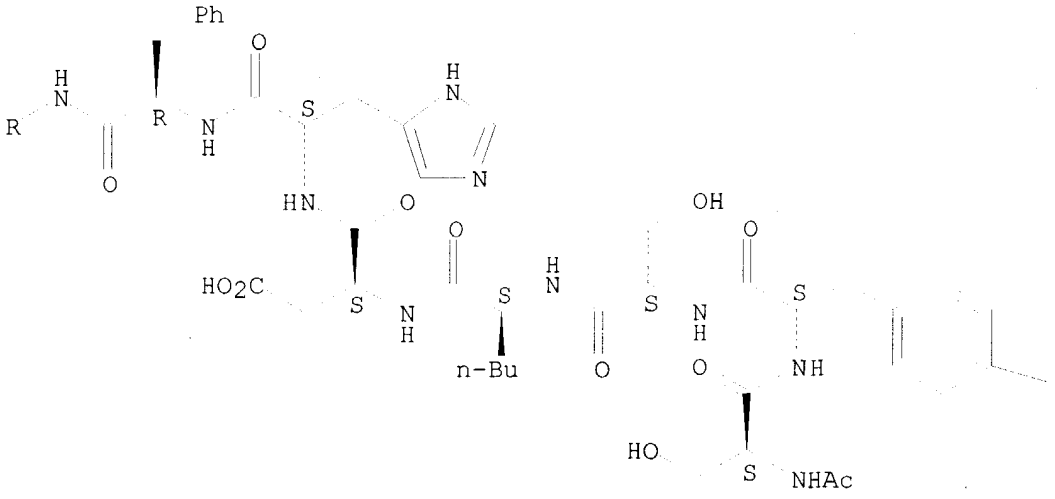
CN L-Valinamide, N-acetyl-L-seryl-L-tyrosyl-L-seryl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-L-lysylglycyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



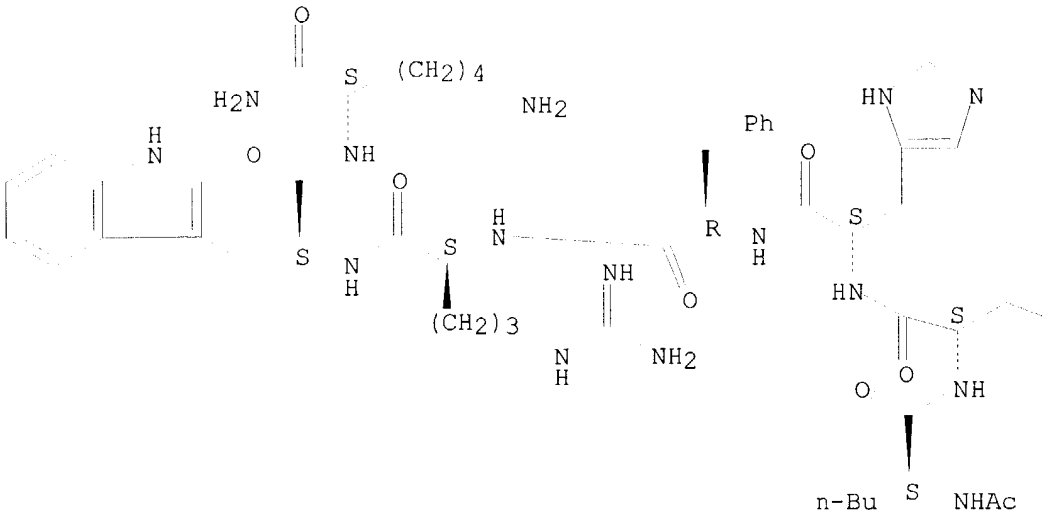
PAGE 2-B

OH

RN 117499-53-3 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



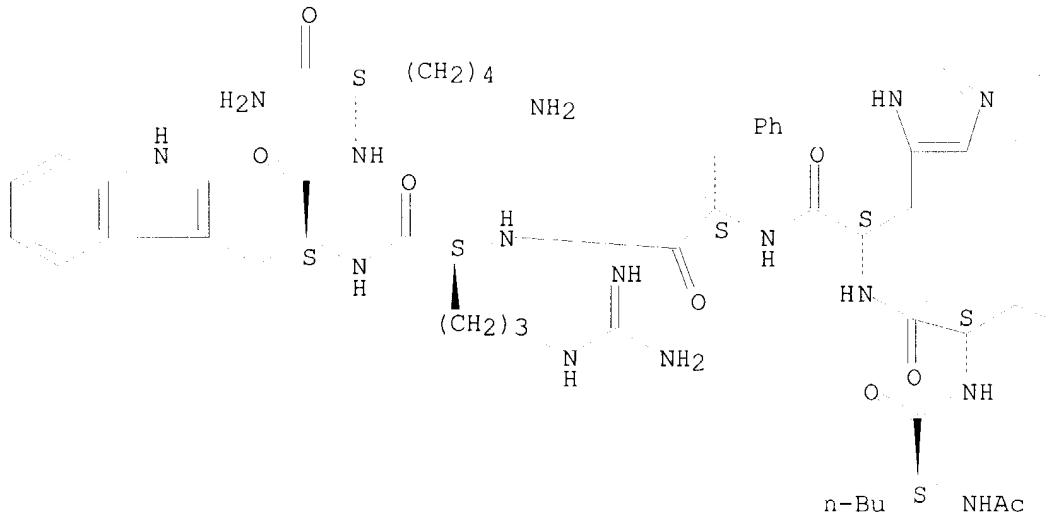
PAGE 1-B

CO_2H

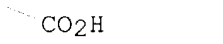
RN 117603-87-9 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-L-phenylalanyl-L-arginyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



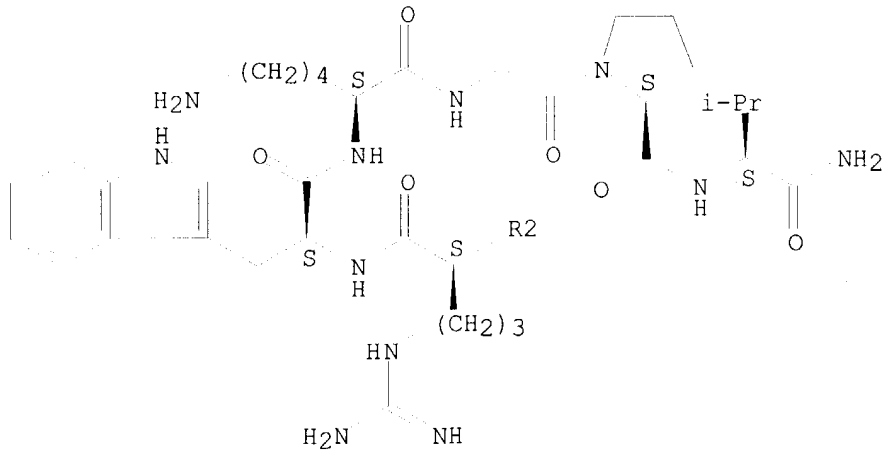
PAGE 1-B



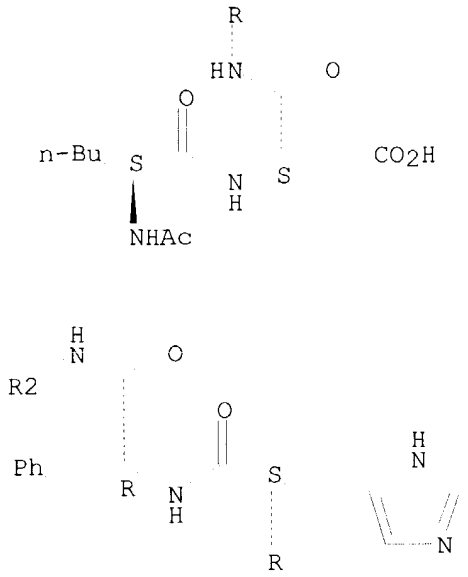
RN 121062-05-3 HCAPLUS
CN L-Valinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-L-lysylglycyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



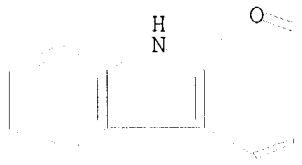
PAGE 2-A



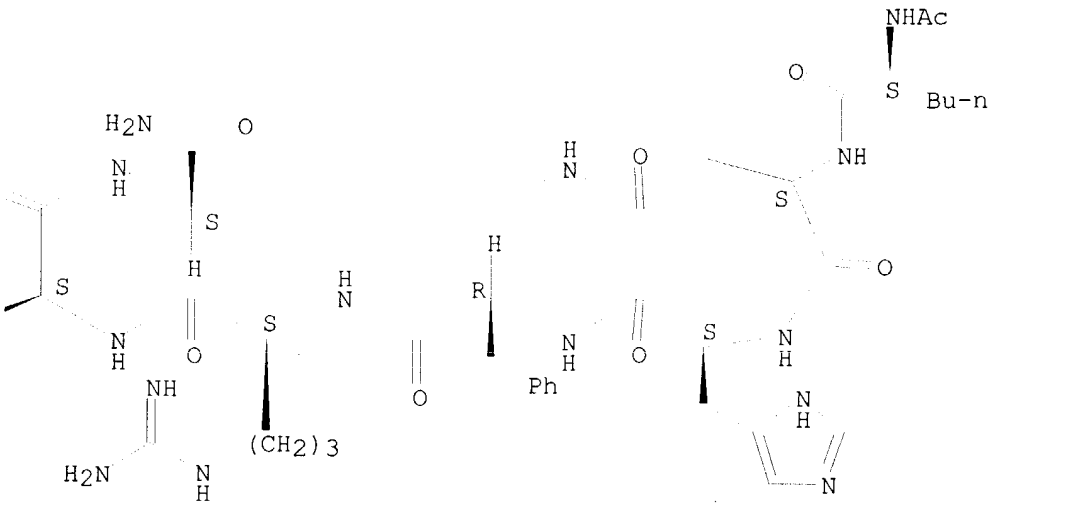
RN 121062-08-6 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L15 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:507697 HCAPLUS
DOCUMENT NUMBER: 129:245475
TITLE: Synthesis of **cyclic** α-MSH **peptides**
AUTHOR(S): Schaaper, Wim M. M.; Adan, Roger A. H.; Posthuma, Truus A.; Oosterom, Julia; Gispen, Willem-Hendrik; Meloen, Rob H.
CORPORATE SOURCE: ID-DLO, Institute for Animal Science and Health, Lelystad, 8200 AB, Neth.
SOURCE: Letters in Peptide Science (1998), 5(2-3), 205-208
CODEN: LPSCEM; ISSN: 0929-5666
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cyclic analogs of α-MSH(1-13) and of α-MSH(4-10) have been synthesized. The peptides were synthesized using Fmoc chemical, and improvements in the cyclization step were made. For example, side chains of Asp5 and Lys10 in the deprotected peptide were coupled in DMF to form a cyclic lactam, using an excess of PyBOP reagent and DIEA as a base. The cyclization reaction was completed within 1 h and was almost quant. A cyclic analog of α-MSH, containing a disulfide bridge, was also synthesized. The peptides were tested for their selectivity for the rat MC4 receptor. Substitution of Phe7 of α-MSH, and cyclization of the peptide dramatically influenced the selectivity for the rMC4 receptor.

IT **168482-23-3P**, MBX 36 **213314-48-8P**, MBJ 07
213314-49-9P, MBX 37
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of **cyclic** α-MSH **peptides**)

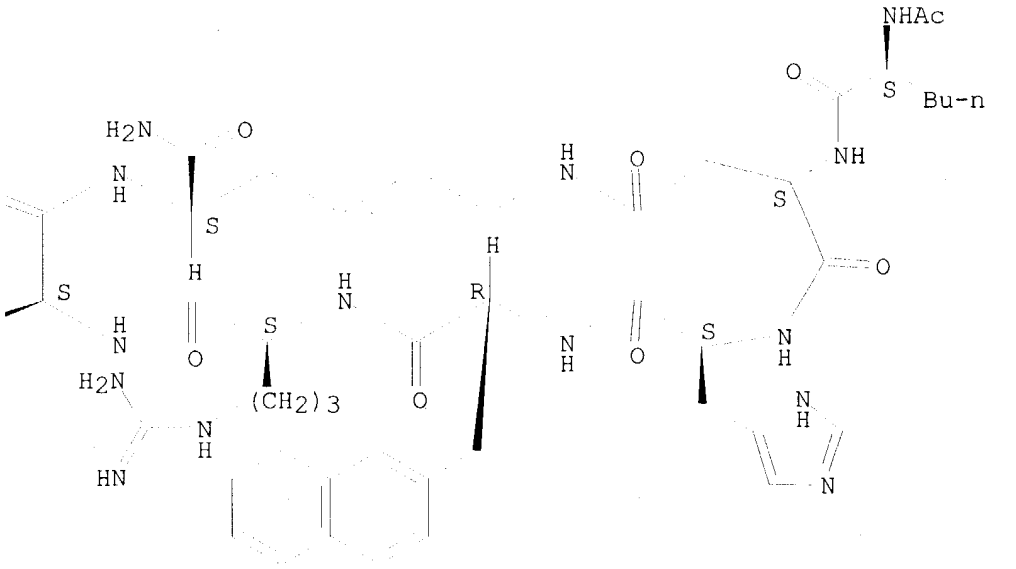
RN 168482-23-3 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-3-(2-naphthalenyl)-D-alanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI)

(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A

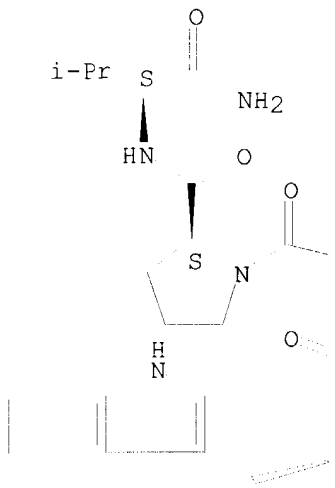
PAGE 1-B



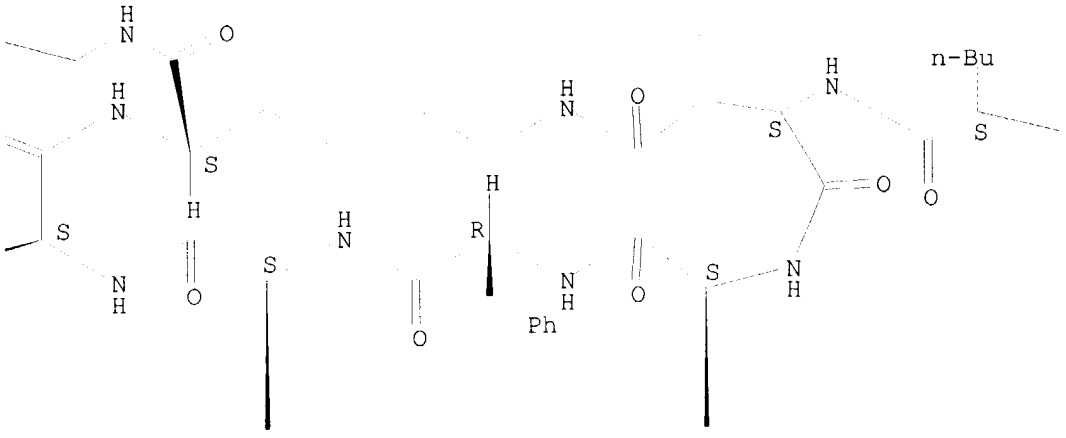
RN 213314-48-8 HCAPLUS
CN L-Valinamide, N-acetyl-L-seryl-L-tyrosyl-L-seryl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-L-lysylglycyl-L-prolyl-, (5→10)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

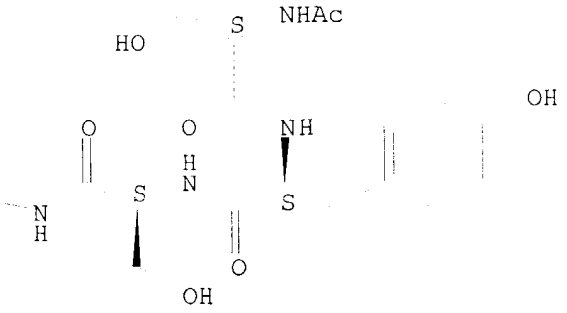


PAGE 1-B



Search completed by David Schreiber x22526

PAGE 1-C

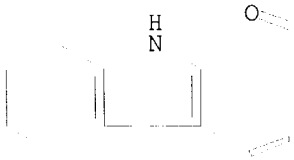


PAGE 2-B

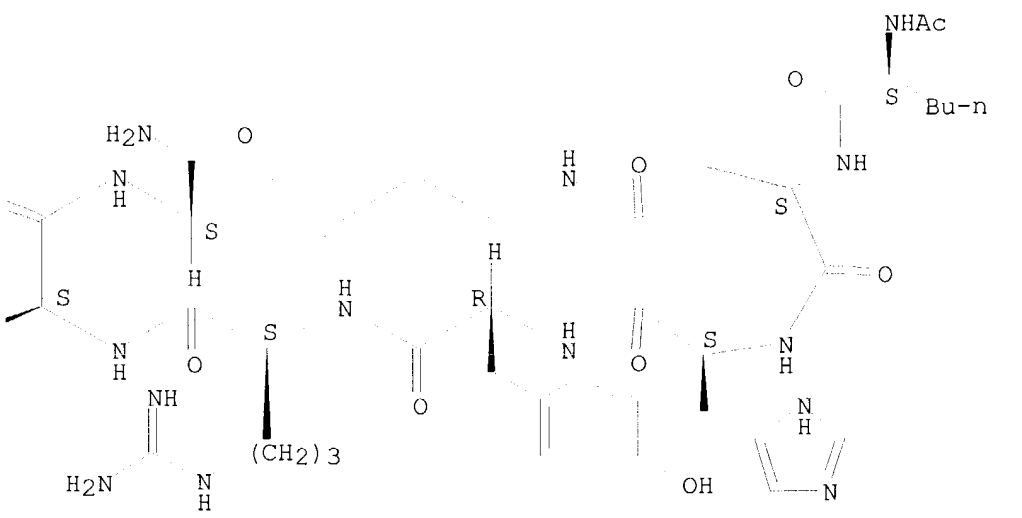
RN 213314-49-9 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-tyrosyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



Search completed by David Schreiber x22526



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:34211 HCAPLUS
DOCUMENT NUMBER: 128:190087
TITLE: Octanol-water partition of nonzwitterionic peptides: predictive power of a molecular size-based model
AUTHOR(S): Buchwald, Peter; Bodor, Nicholas
CORPORATE SOURCE: Center for Drug Discovery, University of Florida, Health Science Center, Gainesville, FL, 32610-0497, USA
SOURCE: Proteins: Structure, Function, and Genetics (1998), 30(1), 86-99
CODEN: PSFGEY; ISSN: 0887-3585
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

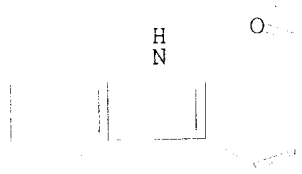
AB A remarkably simple, mol. size-based model developed to predict octanol-water partition coeffs. for organic compds. is tested on a set of 188 neutral peptides with available exptl. partition data. Despite using only two parameters, it gives a promising correlation ($r2 = 0.914$; $\sigma = 0.455$, $F = 1978.0$), and predictions are in a realistic range even for larger peptides (cyclosporin, melanotan, sandostatin) where common, overparametrized fragment methods become quite unreliable. Ion-pair partitioning and the extraction constant formalism is briefly reviewed to describe the sigmoidal lipophilicity profile of ionizable, nonzwitterionic peptides. It seems possible to extend the present model to estimate apparent partition coeffs. measured around neutral pH and physiol. conditions for monoionic peptides; however, as no standard conditions are yet defined and only relatively small number of exptl. data are available, the situation here is more complex.

IT **121062-08-6**, Melanotan II
RL: PRP (Properties)
(octanol-water partition of nonzwitterionic peptides and predictive power of mol. size-based model)

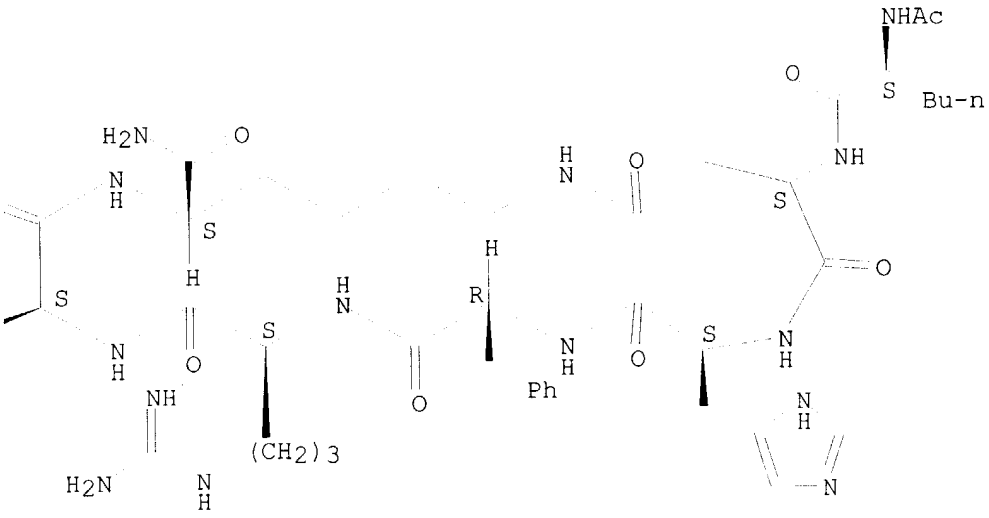
RN 121062-08-6 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:735794 HCAPLUS
DOCUMENT NUMBER: 127:346663
TITLE: Preparation and biological activity of cyclic bridged α-MSH analogs
INVENTOR(S): Hadley, Mac E.; Hruby, Victor J.; Sharma, Shubh D.
PATENT ASSIGNEE(S): Competitive Technologies, Inc., USA
SOURCE: U.S., 9 pp., Cont.-in-part of U.S. Ser. No. 199,775, abandoned.

Search completed by David Schreiber x22526

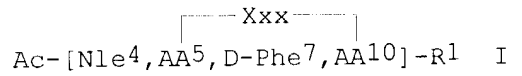
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5683981	A	19971104	US 1995-470343	19950606
US 5674839	A	19971007	US 1994-349902	19941206
US 5714576	A	19980203	US 1997-826676	19970407

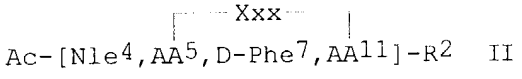
PRIORITY APPLN. INFO.:

US 1987-53229 B2 19870522
US 1988-212807 B1 19880629
US 1990-611456 B2 19901113
US 1992-938781 B1 19920831
US 1994-199775 B2 19940222
US 1992-916767 B1 19920717
US 1994-349902 A3 19941206

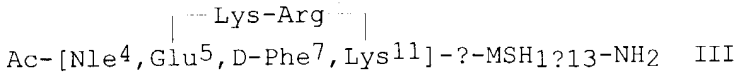
GI



I



II



III

AB Novel cyclic bridged α-MSH analogs I and II (AA5, AA10, AA11 = L- or D-amino acid containing ω-amino or carboxyl group in the side chain; Xxx = 1-5 α-amino acid residues, each of which may be of L- or D-configuration, or linear or branched spacer chain containing terminal amino and/or carboxy groups; R1, R2 designates α-MSH1-13NH2, α-MSH1-12NH2, α-MSH1-11NH2, α-MSH4-13NH2, α-MSH4-10NH2) are described herein. With the described analogs, when administered in pharmaceutical compns., it is now possible to achieve normalization of hypopigmentation dysfunctions and to achieve darkening of the skin in the total absence of sun or UV light irradiation Thus, **cyclic peptide** III was prepared by standard solid-phase methods and displayed α-MSH relative potencies of 100 in a frog skin assay and 5 in a lizard skin assay.

IT **198267-22-0P**, SHU 9020 **198267-23-1P**, SHU 9021
198267-25-3P, SHU 9018
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of cyclic bridged α-MSH analogs)

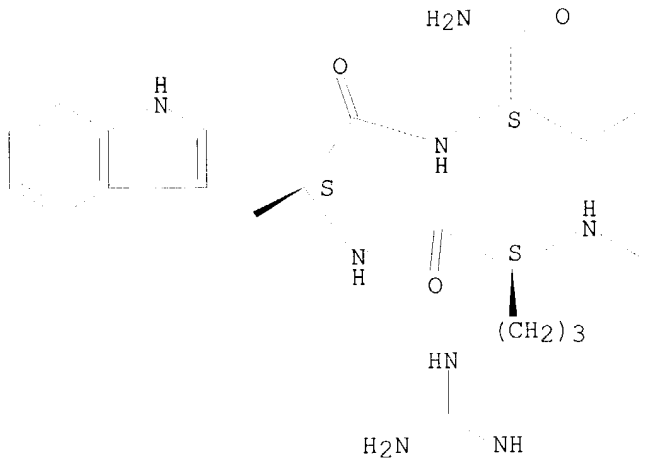
RN 198267-22-0 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-

Search completed by David Schreiber x22526

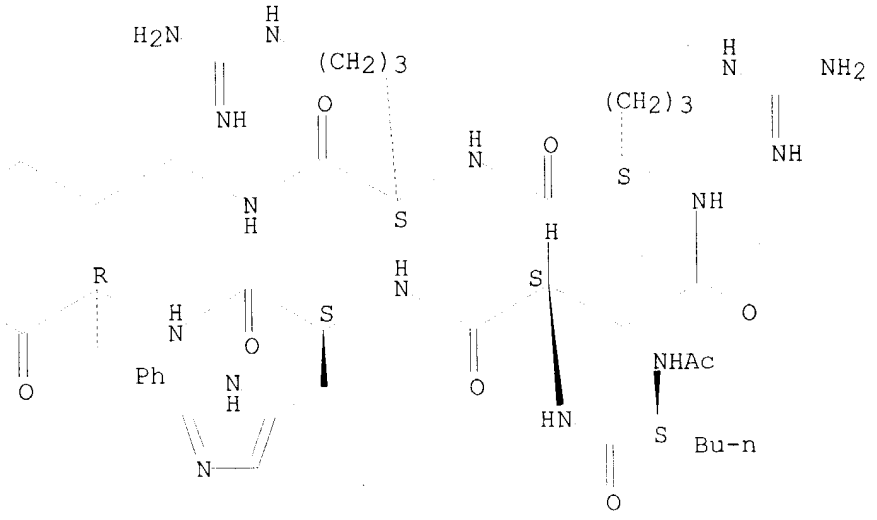
phenylalanyl-L-arginyl-L-tryptophyl-N6-(L-arginyl-L-arginyl)-,
(2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



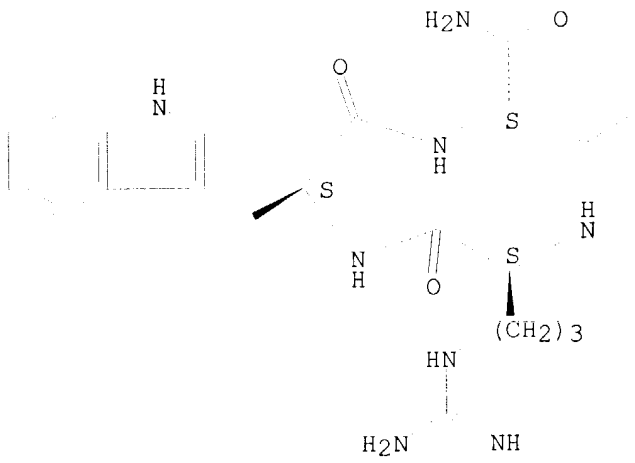
PAGE 1-B



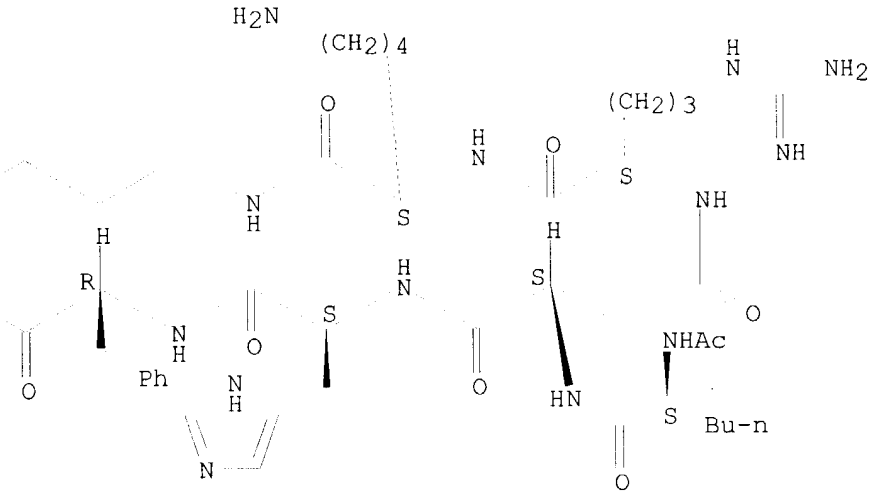
RN 198267-23-1 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-N6-(L-arginyl-L-lysyl)-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



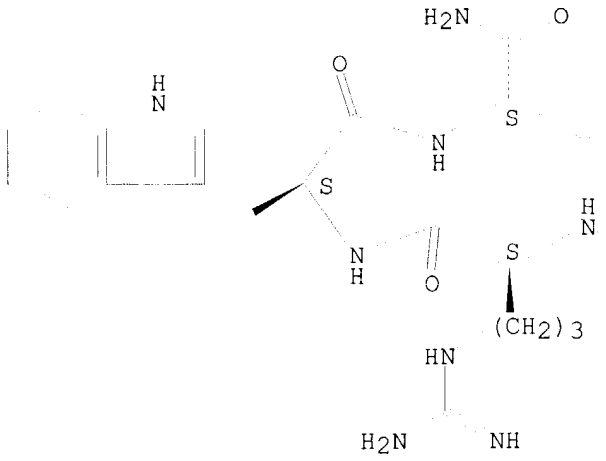
PAGE 1-B



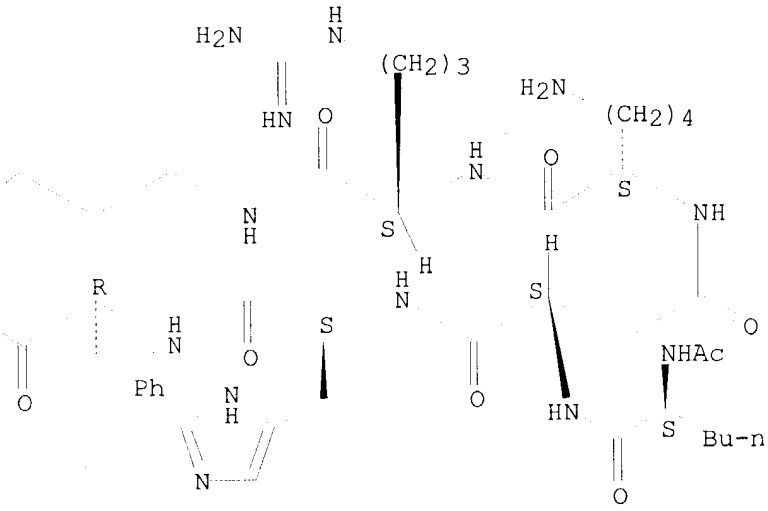
RN 198267-25-3 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-N6-(L-lysyl-L-arginyl)-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L15 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:483379 HCAPLUS
DOCUMENT NUMBER: 127:117483
TITLE: β-Methylation of the Phe7 and Trp9 melanotropin side chain pharmacophores affects ligand-receptor interactions and prolonged biological activity
AUTHOR(S): Haskell-Luevano, Carrie; Toth, Kate; Boteju, Lakmal; Job, Constatin; de Castrucci, Ana Maria; Hadley, Mac E.; Hruby, Victor J.
CORPORATE SOURCE: Departments of Chemistry and Anatomy, University of

Search completed by David Schreiber x22526

Arizona, Tucson, AZ, 85721, USA
SOURCE: Journal of Medicinal Chemistry (1997), 40(17), 2740-2749
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Topog. modified melanotropin side chain pharmacophore residues Phe7 and Trp9 in a **cyclic peptide** template (Ac-Nle4-c[Asp-His-Xaa7-Arg-Yaa9-Lys]-NH2) and Phe7 in a linear peptide template (Ac-Ser-Tyr-Ser-Nle4-Glu-His-Xaa7-Arg-Trp-Gly-Lys-Pro-Val-NH2) result in differences in potency and prolonged biol. activity in the frog and lizard skin bioassays. These topog. modifications included the four isomers of β-methylphenylalanine (β-MePhe)7 and β-methyltryptophan (β-MeTrp)9 and the two isomers of 1,2,3,4-tetrahydro-β-carboline (Tca).9. Modifications in the cyclic template resulted in up to a 1000-fold difference in potency for the β-MePhe7 stereoisomeric peptides; up to a 476-fold difference in potency resulted for the β-MeTrp9 peptides, and about a 50-fold difference between the Tca9-containing peptides. Up to a 40-fold difference in potency resulted for the β-MePhe7 stereoisomeric peptides using the linear template in these assays. The relative potency ranking for modifications in the cyclic template of β-MePhe7 were 2R,3S > 2S,3S = 2S,3R > 2R,3R in the frog assay and 2S,3R > 2R,3S > 2S,3S > 2R,3R in the lizard assay. The relative potencies for modifications in the cyclic template of β-MeTrp9 were 2R,3S > 2R,3R > 2S,3S » 2S,3R in the frog assay and 2S,3S = 2R,3R > 2R,3S > 2S,3R in the lizard assay. The relative potencies for modifications in the cyclic template of Tca9 were DTca > LTca in both assays. Significant differences in prolonged (residual) activities were also observed for these modified peptides and were dependent upon stereochem. of the β-Me amino acid, peptide template, and bioassay system. Furthermore, comparisons of β-MeTrp9 stereoisomeric peptides on the frog, lizard, and human MC1 receptors suggest that structure-activity relationships on both the classical frog and lizard skin bioassays do not necessarily predict corresponding SAR profiles for the human melanocortin receptors, indicating a remarkable species specificity of the MC1 receptor requirements.

IT **121062-08-6 166255-31-8 166255-32-9**
166255-33-0 166255-34-1 169056-23-9
192646-24-5 192646-25-6 192646-26-7
192646-27-8 192646-28-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(β-methylation of the Phe7 and Trp9 melanotropin side chain pharmacophores affects ligand-receptor interactions and prolonged biol. activity)

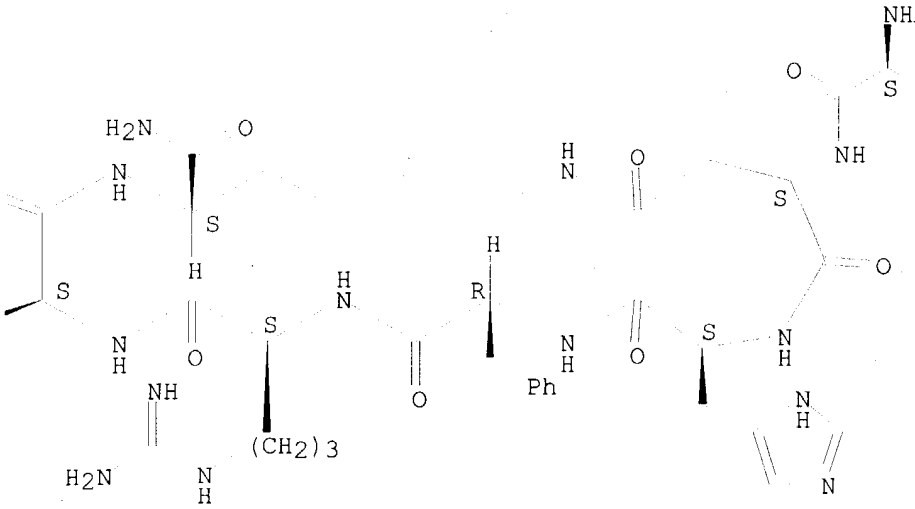
RN 121062-08-6 HCAPLUS

CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

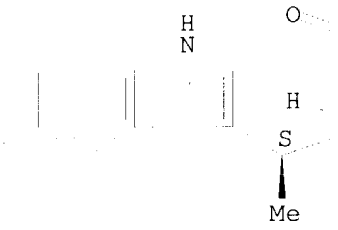
PAGE 1-B



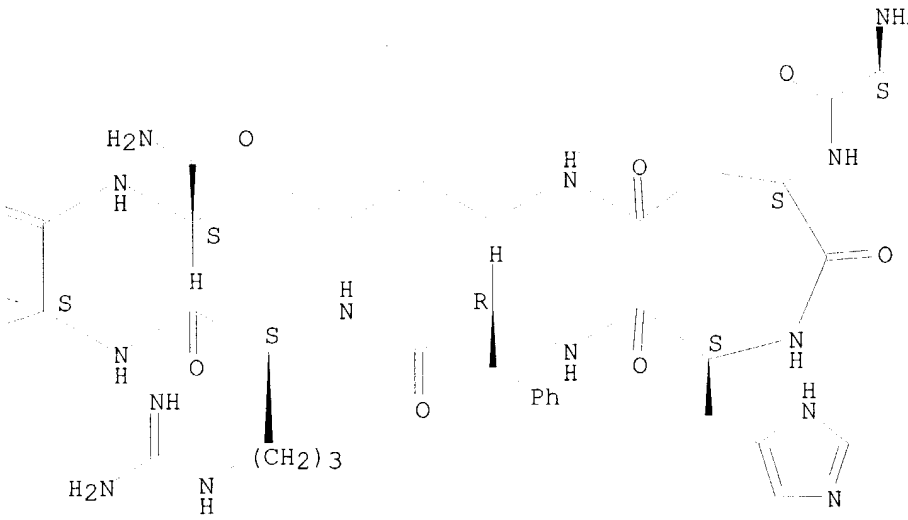
RN 166255-31-8 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-(βS)-β-methyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



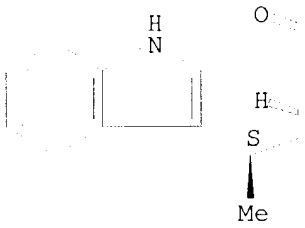
PAGE 1-B



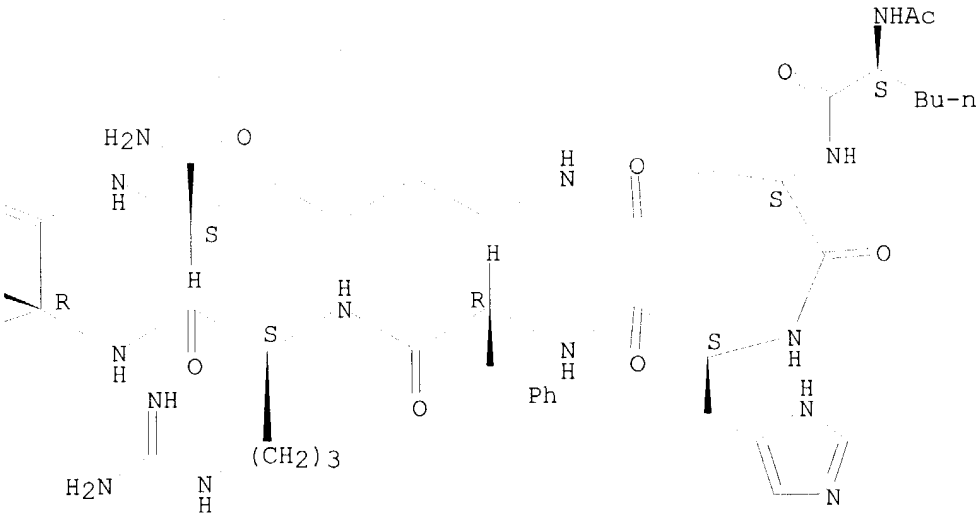
RN 166255-32-9 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-(βS)-β-methyl-D-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



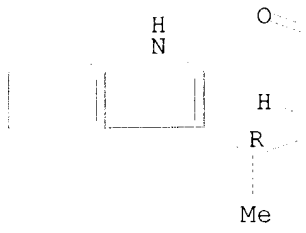
PAGE 1-B



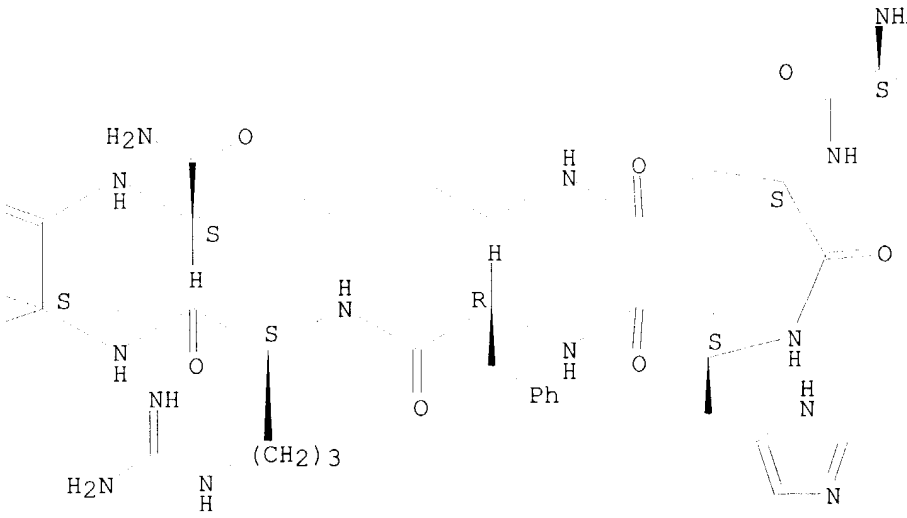
RN 166255-33-0 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-(βR)-β-methyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



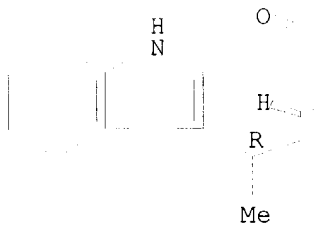
PAGE 1-B



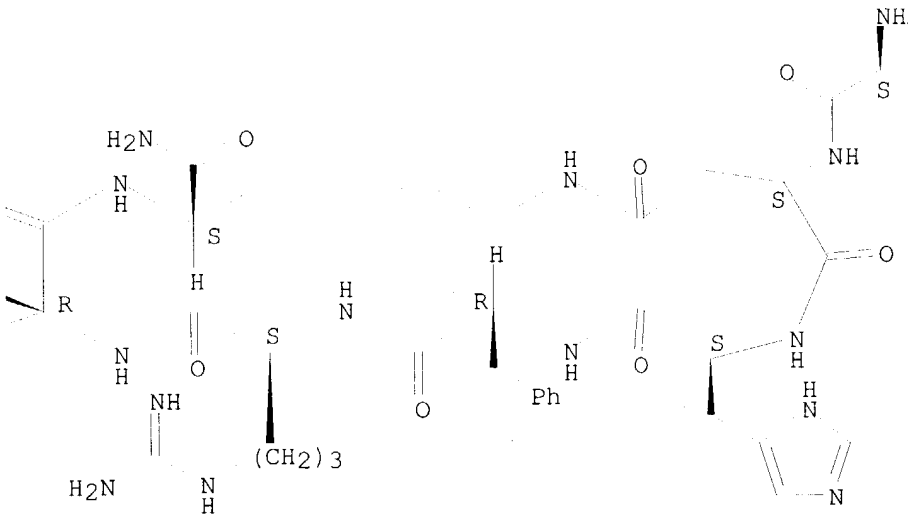
RN 166255-34-1 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-(βR)-β-methyl-D-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



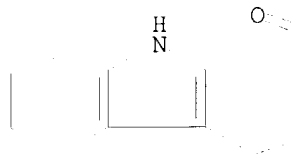
PAGE 1-B



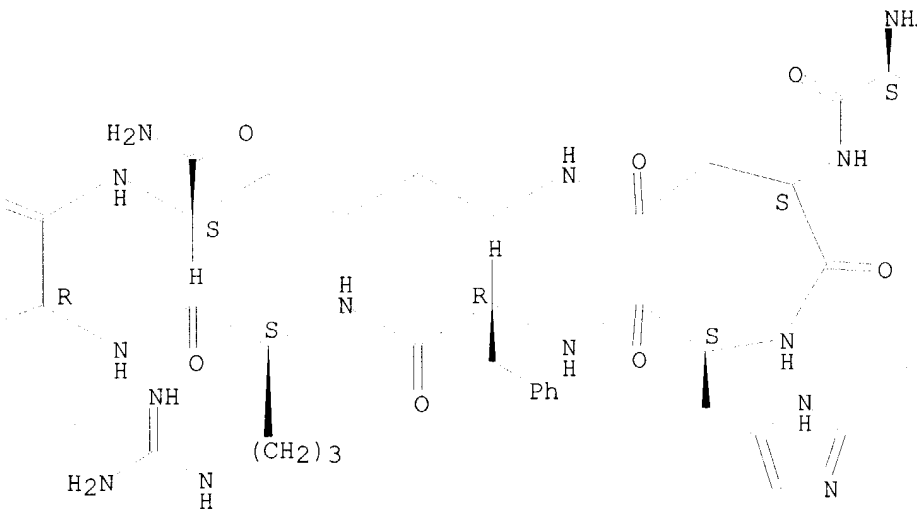
RN 169056-23-9 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-D-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RN 192646-24-5 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-L-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

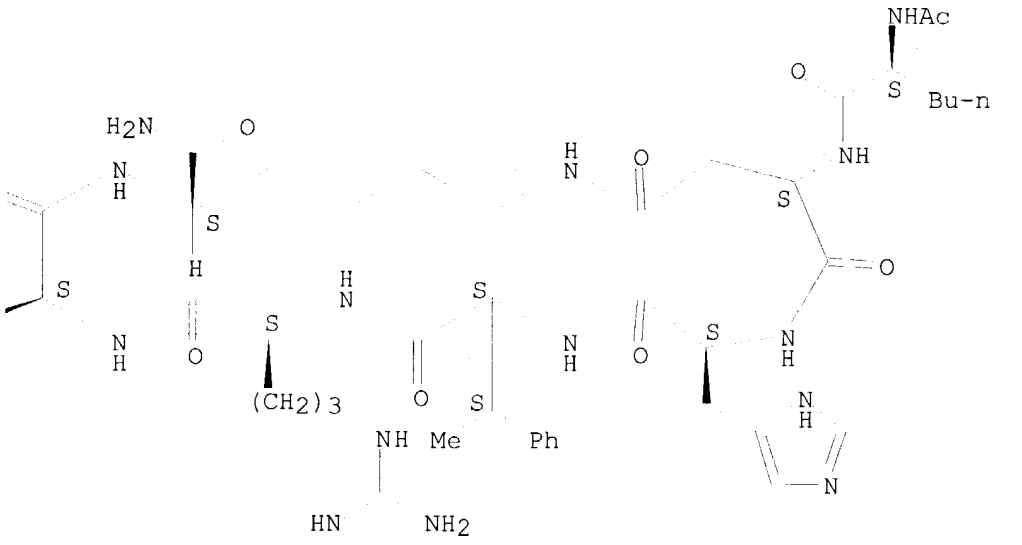
PAGE 1-B

RN 192646-25-6 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-(βS)-β-methyl-L-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

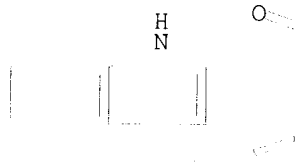
PAGE 1-B



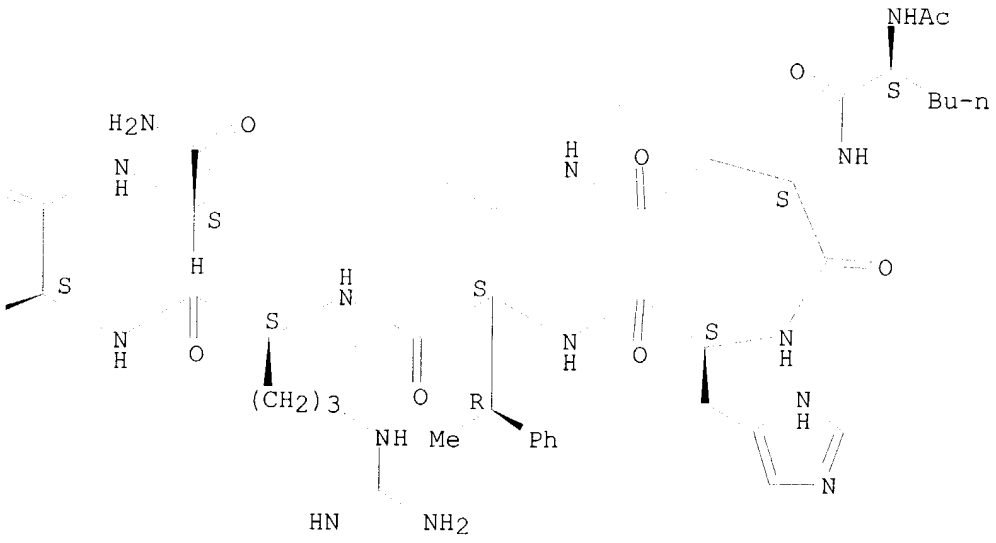
RN 192646-26-7 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-(βR)-β-methyl-L-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



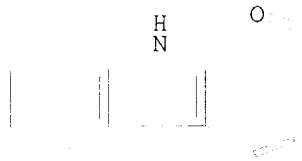
PAGE 1-B



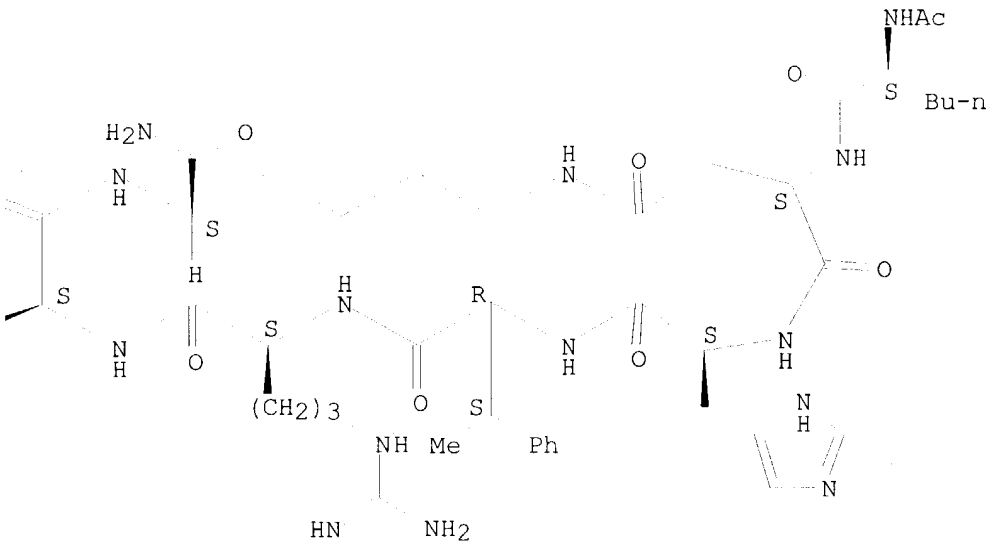
RN 192646-27-8 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-(βS)-β-methyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



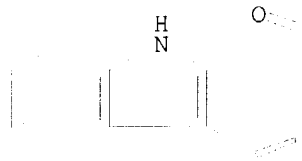
PAGE 1-B



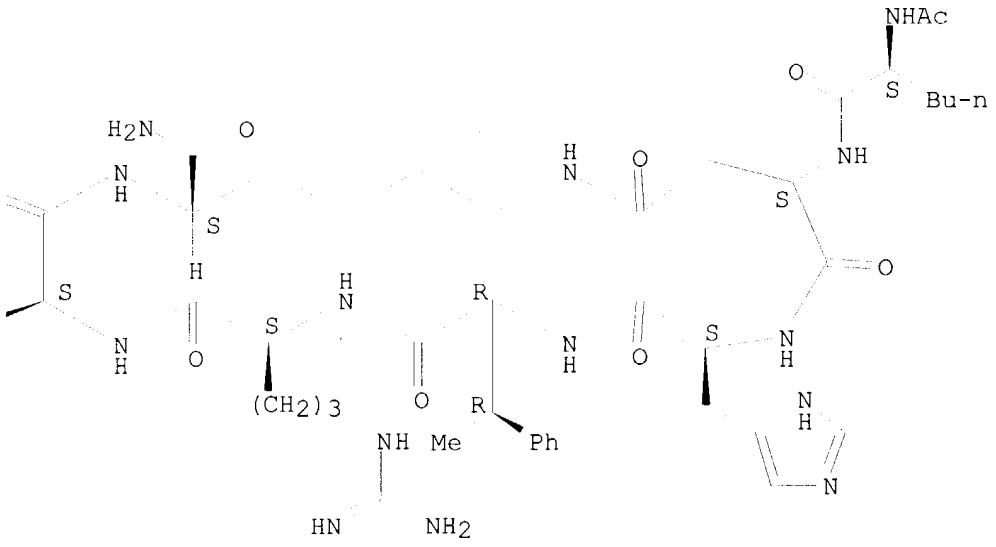
RN 192646-28-9 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-(βR)-β-methyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L15 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:310073 HCAPLUS
DOCUMENT NUMBER: 126:325679
TITLE: Biological and Conformational Examination of Stereochemical Modifications Using the Template Melanotropin Peptide, Ac-Nle-c[Asp-His-Phe-Arg-Trp-Ala-Lys]-NH2, on Human Melanocortin Receptors
AUTHOR(S): Haskell-Luevano, Carrie; Nikiforovich, Gregory; Sharma, Shubh D.; Yang, Ying-Kui; Dickinson, Chris; Hruby, Victor J.; Gantz, Ira
CORPORATE SOURCE: Departments of Internal Medicine Pediatrics and Surgery, University of Michigan Medical Center, Ann Arbor, MI, 48109, USA
SOURCE: Journal of Medicinal Chemistry (1997), 40(11), 1738-1748
CODEN: JMCMAR; ISSN: 0022-2623

Search completed by David Schreiber x22526

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Examination of conformationally constrained melanotropin peptides (Ac-Nle4-c[Asp5-His-Phe7-Arg-Trp9-Ala-Lys]-NH2) on four human melanotropin receptors (hMC1R, hMC3R, hMC4R, and hMC5R) resulted in identifying the importance of ligand stereochem. at positions 5, 7, and 9 for agonist binding affinity and receptor selectivity. A trend in ligand structure-activity relationships emerged for these peptides, with the hMC1R and hMC4R possessing similar tendencies, as did the hMC3R and hMC5R. α-MSH (Ac-Ser-Tyr-Ser-Met4-Glu-His-Phe7-Arg-Trp-Gly-Lys-Pro-Val-NH2), NDP-MSH (Ac-Ser-Tyr-Ser-Nle4-Glu-His-d-Phe7-Arg-Trp-Gly-Lys-Pro-Val-NH2) and MTII (Ac-Nle4-c[Asp5, d-Phe7, Lys10]-NH2) were also examined at each of these melanocortin receptors. Interestingly, the linear NDP-MSH possessed greater binding affinity for the hMC3R and hMC5R than did the cyclic analog MTII. The peptide Ac-Nle-c[Asp-His-Phe-Arg-D-Trp9-Ala-Lys]-NH2 demonstrated the greatest differentiation in binding affinity between the hMC1R and hMC4R (78-fold). Analog Ac-Nle-c[Asp-His-Phe7-Arg-Trp-Ala-Lys]-NH2 resulted in micromolar binding affinity (or greater) at the hMC3R and hMC5R, demonstrating the importance of D-Phe7 for ligand binding potency at these receptors. Ac-c[Asp-His-Phe-Arg-Trp-Ala-Lys]-NH2 resulted in loss of binding affinity at the hMC5R, implicating the importance of Nle4 (or a hydrophobic residue in this position) for binding to this receptor. Ac-Nle-c[D-Asp5-His-Phe-Arg-Trp-Ala-Lys]-NH2 was unable to competitively displace [125I]NDP-MSH binding at micromolar concns. on the hMC3R and hMC5R, suggesting the importance of chirality of Asp5 either for ligand-receptor interactions or for orientation of the side chain lactam bridge and the structural integrity of the peptide conformation. Energy calcns. performed for these peptides resulted in the identification of a low-energy ligand conformer family that is common to all the ligands. The differences in ligand binding affinities observed in this study are postulated to be a result of different ligand-receptor complexed interactions and not solely to the ligand structure.

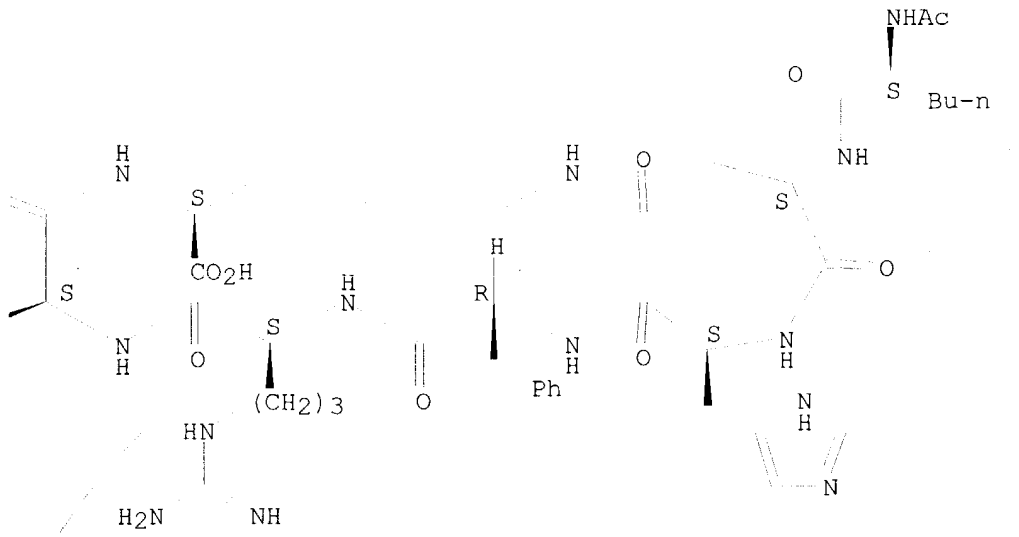
IT **189691-06-3**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(biol. and conformational examination of stereochem. modifications using a template melanotropin peptide on human melanocortin receptors)

RN 189691-06-3 HCAPLUS

CN L-Lysine, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B



L15 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:193328 HCAPLUS
DOCUMENT NUMBER: 126:272459
TITLE: Characterization of D117A and H260A mutations in the melanocortin 1 receptor
AUTHOR(S): Schioeth, Helgi B.; Muceniece, Ruta; Szardenings, Michael; Prusis, Peteris; Lindeberg, Gunnar; Sharma, Shubh D.; Hruby, Victor J.; Wikberg, Jarl E. S.
CORPORATE SOURCE: Dep. Pharmaceutical Pharmacology, Uppsala Univ., Uppsala, Swed.
SOURCE: Molecular and Cellular Endocrinology (1997), 126(2), 213-219
CODEN: MCEND6; ISSN: 0303-7207
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

QP187.A1463

AB Recent site directed mutagenesis studied on the melanocortin 1 (MC1) receptor have indicated the importance of D117 and H260 amino acid residues for the binding of α-MSH. Here, the authors report the testing of 12 **cyclic** and linear MSH **peptides** on the D117A and H260A mutant receptors. Moreover, the authors constructed a double mutant which displayed a major loss in affinity for [Nle4,D-Phe7]α-MSH. New data of His6 and Phe7 substituted MSH peptides are compared with previous results and the hypothesis of putative interactions of D117 and H260 with single amino acids in the MSH peptide. The conclusions are that the D117A and the H260A mutations may cause conformational changes in the receptor which can not be linked to any specific amino acid in the MSH-peptides.

IT **188981-70-6 188981-71-7**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α-MSH analog binding and characterization of D117A and H260A

Search completed by David Schreiber x22526

mutations in melanocortin 1 receptor)

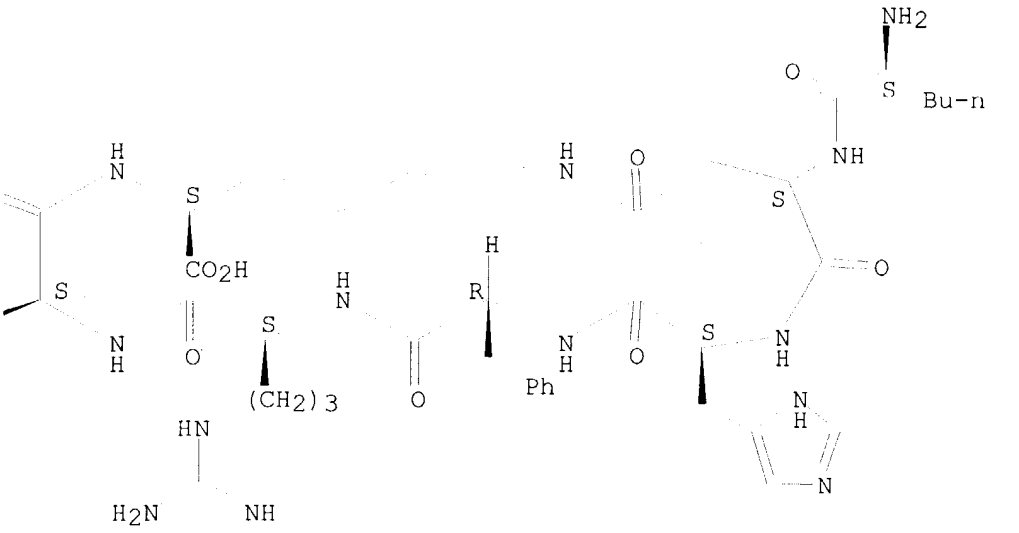
RN 188981-70-6 HCAPLUS

CN L-Lysine, L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

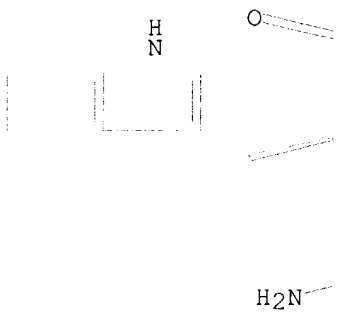


RN 188981-71-7 HCAPLUS

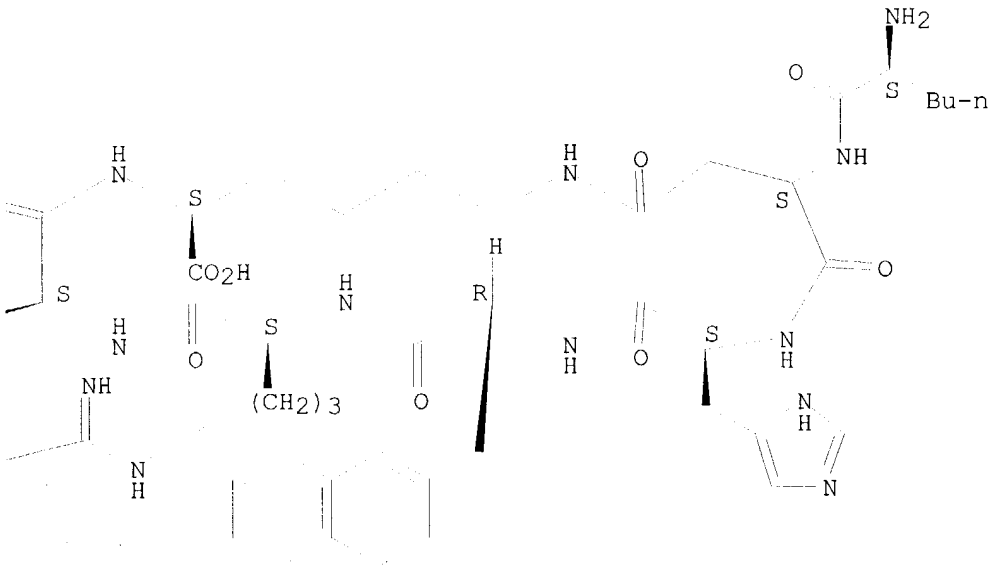
CN L-Lysine, L-norleucyl-L-α-aspartyl-L-histidyl-3-(2-naphthalenyl)-D-alanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L15 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:250787 HCAPLUS
DOCUMENT NUMBER: 124:279637
TITLE: Evaluation of Melanotan-II, a superpotent **cyclic** melanotropic **peptide** in pilot phase-I clinical study
AUTHOR(S): Dorr, Robert T.; Lines, Ruskin; Levine, Norman; Brooks, Christine; Xiang, Li; Hruby, Victor J.; Hadley, Mac E.

Search completed by David Schreiber x22526

CORPORATE SOURCE: Coll. Med., Univ. Arizona, Tucson, AZ, USA
SOURCE: Life Sciences (1996), 58(20), 1777-84
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

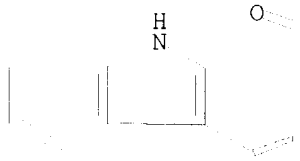
AB A pilot phase I study was conducted with a cyclic heptapeptide analog of α-MSH. The lactam-bridged mol., called Melanotan-II (MT-II), has the structure Ac-Nle4-Asp5-His6-D-Phe7-Arg8-Trp9-Lys10α-MSH4-10-NH2 and has superpotent melanotropic activity in vitro. A single-blind, alternating day (saline or MT-II), placebo-controlled trial was conducted in 3 normal male volunteers at the starting dose of 0.01 mg/kg of MT-II. S.c. injections of MT-II or saline were given daily (Monday-Friday) for 2 consecutive weeks. Two subjects were escalated by 0.005 mg/kg increments to 0.03 mg/kg and one to 0.025 mg/kg. The 0.03 mg/kg dose produced Grade II somnolence and fatigue in one of two subjects (WHO stds.). Mild nausea, not requiring antiemetic treatment, was reported at most MT-II dose levels. A stretching and yawning complex appeared to correlate with the onset of spontaneous, penile erections which were intermittently experienced for 1-5 h after MT-II dosing, depending on the MT-II dose. Two subjects had increased pigmentation in the face, upper body and buttock as measured by quant. reflectance and by visual perception 1 wk after MT-II dosing ended. These results demonstrate that MT-II has tanning activity in humans given only 5 low doses every other day by s.c. injection. The recommended single MT-II dose for future Phase I studies is 0.025 mg/kg/day.

IT **121062-08-6**, Melanotan-II
RL: ADV (Adverse effect, including toxicity); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(tanning activity and side effects in clin. study of Melanotan-II, a superpotent **cyclic** melanotropic **peptide**, in men)

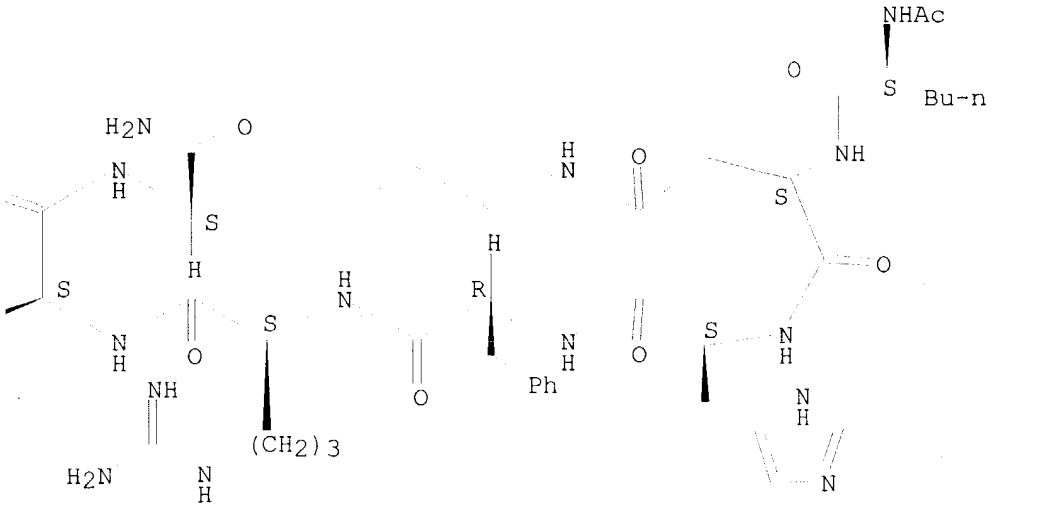
RN 121062-08-6 HCAPLUS

CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B



L15 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:552245 HCAPLUS
DOCUMENT NUMBER: 119:152245
TITLE: A conformational study of two **cyclic peptide** analogs of α-MSH
AUTHOR(S): Forsyth, George; Branch, Sarah; Moss, Stephen; Notarianni, Lidia; Osguthorpe, David; Pouton, Colin
CORPORATE SOURCE: Sch. Pharm. Pharmacol., Univ. Bath, Bath, BA2 7AY, UK
SOURCE: Annals of the New York Academy of Sciences (1993), 680(Melanotropic Peptides), 517-19
CODEN: ANYAA9; ISSN: 0077-8923
DOCUMENT TYPE: Journal
LANGUAGE: English

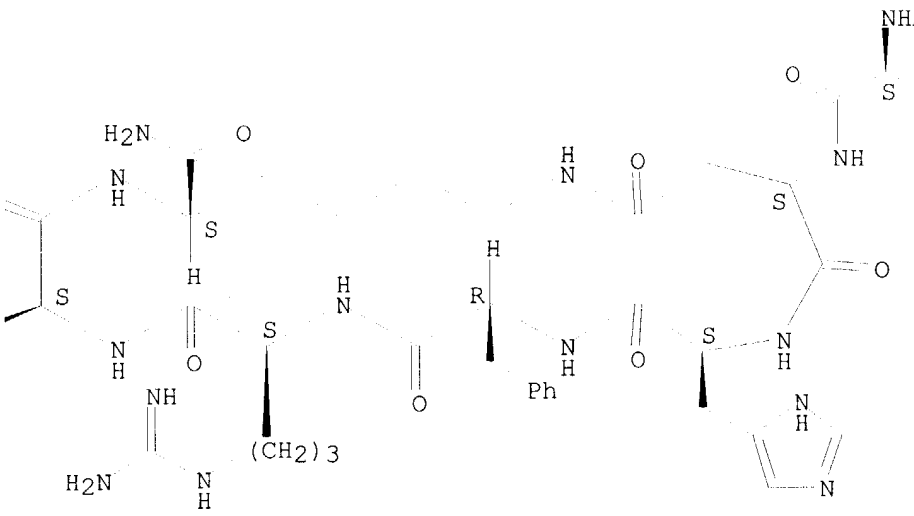
AB Lowest energy conformations were determined for 2 **cyclic peptide** analogs of α-MSH by utilizing mol. dynamic simulations. Such studies have implications in the mol. modeling and computer-assisted design of new analogs.

IT **121062-08-6**
RL: PRP (Properties)
(conformation of)
RN 121062-08-6 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B



L15 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1989:614935 HCAPLUS
DOCUMENT NUMBER:	111:214935
TITLE:	Potent and prolonged-acting cyclic lactam analogs of α-melanotropin: design based on molecular dynamics
AUTHOR(S):	Al-Obeidi, Fahad; Castrucci, Ana M. de L.; Hadley, Mac E.; Hruby, Victor J.
CORPORATE SOURCE:	Dep. Chem., Univ. Arizona, Tucson, AZ, 85721, USA
SOURCE:	Journal of Medicinal Chemistry (1989), 32(12), 2555-61 CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 111:214935

GI

Search completed by David Schreiber x22526

Ac-Ser-Tyr-Ser-Nle-X-His-D-Phe-Arg-Trp-X1-R I

AB Cyclic lactam fragment analogs of α-melanotropin (α-MSH) I (X = Glu, Asp; X1 = Lys, Orn, Dab, Dpr; R = NH2, Gly-Pro-Val-NH2; Dab = 2,4-diaminobutyric acid, Dcpr = 2,3-diaminopropionic acid) were prepared Formation of the lactam bridge between the side-chain groups X and X1 was performed either in solution or on a solid-phase support. The **cyclic peptides** were bioassayed for their melanotropic potency using standard frog (Rana pipiens) and lizard (Anolis carolinensis) skin bioassays. Cyclic melanotropins with 23-membered rings exhibited 100-fold higher melanotropic potency than α-MSH, with selectivity for the lizard melanocyte receptors over the frog melanocyte receptors. Increasing or decreasing the ring size of these cyclic melanotropins diminishes the biol. potency. The 23 and 24-membered ring analogs showed prolonged (residual) biol. activities in both biol. assays, but the smaller ring systems did not. These results provide new insights into the structural and conformational requirements of α-MSH and its analogs at two different types of pigment cell (melanocyte) receptors.

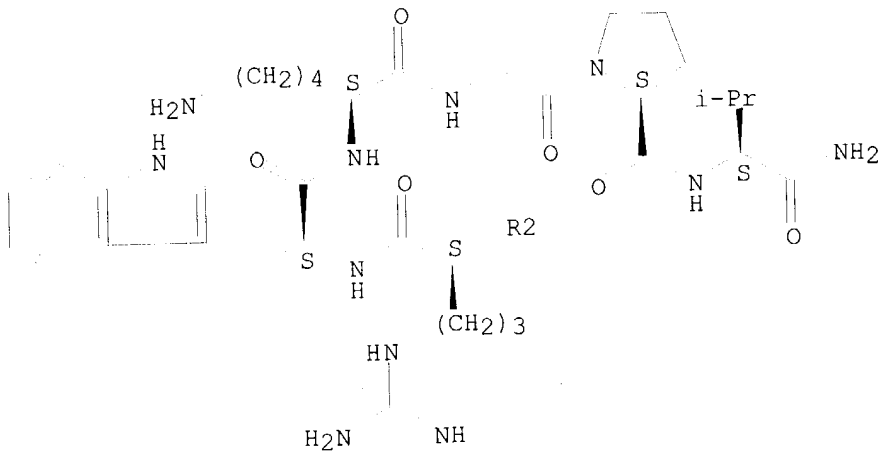
IT **121062-05-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(intramol. lactamization of)

RN 121062-05-3 HCAPLUS

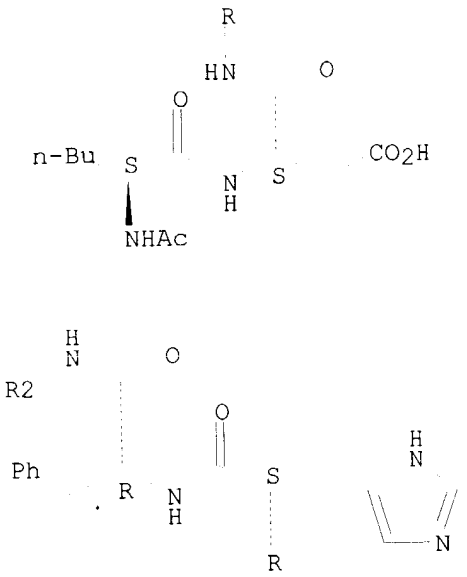
CN L-Valinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-L-lysylglycyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



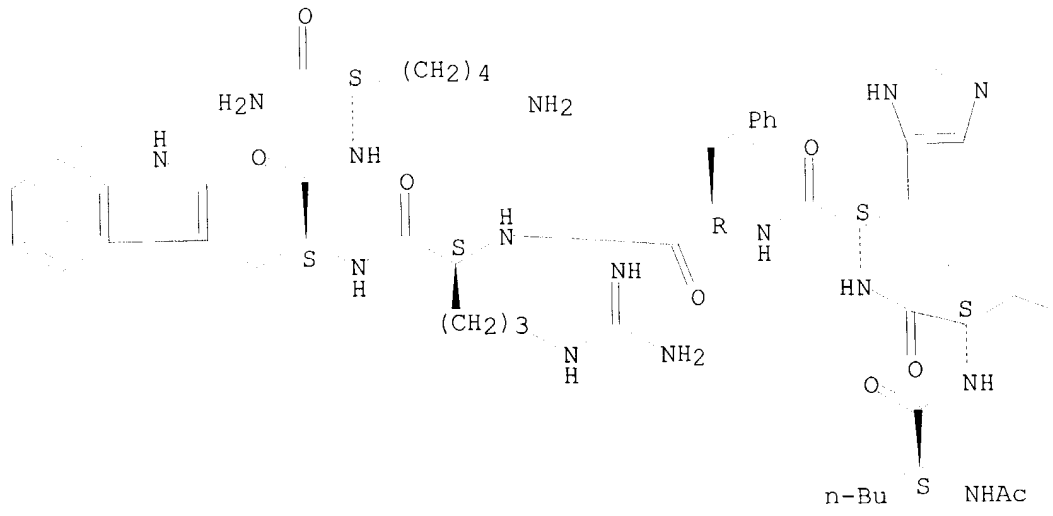
PAGE 2-A



IT **117499-53-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and intramol. lactamization of)
RN 117499-53-3 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



Search completed by David Schreiber x22526

PAGE 1-B

CO_2H

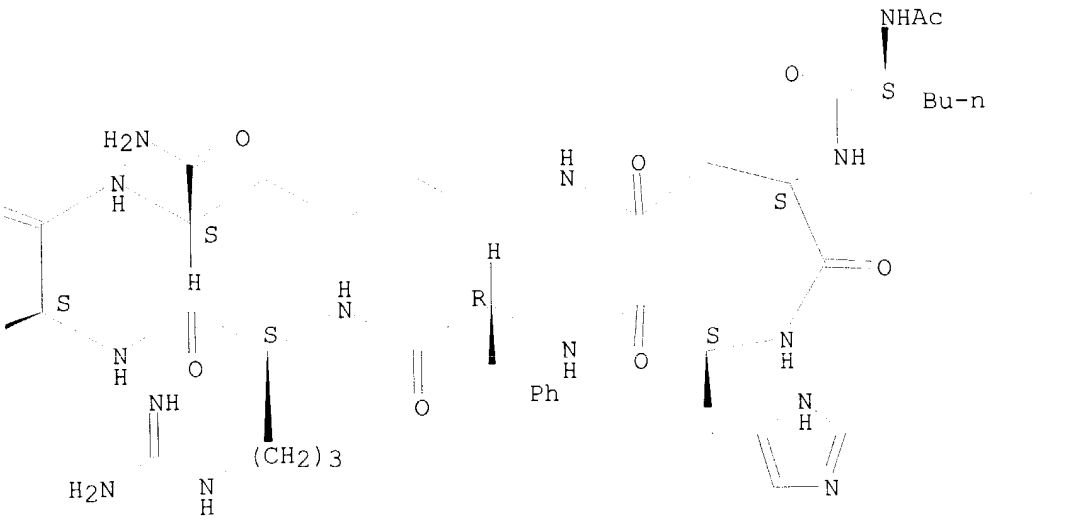
IT **121062-08-6P 122235-72-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and melanotropic activity of)
RN 121062-08-6 HCAPLUS
CN L-Lysinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-, (2→7)-lactam (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

Search completed by David Schreiber x22526

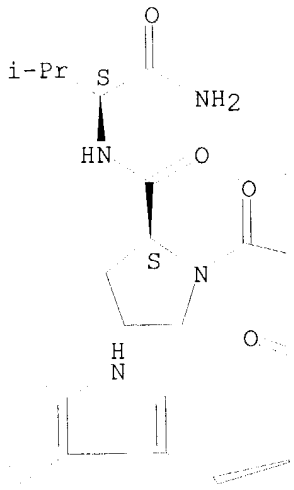
PAGE 1-B



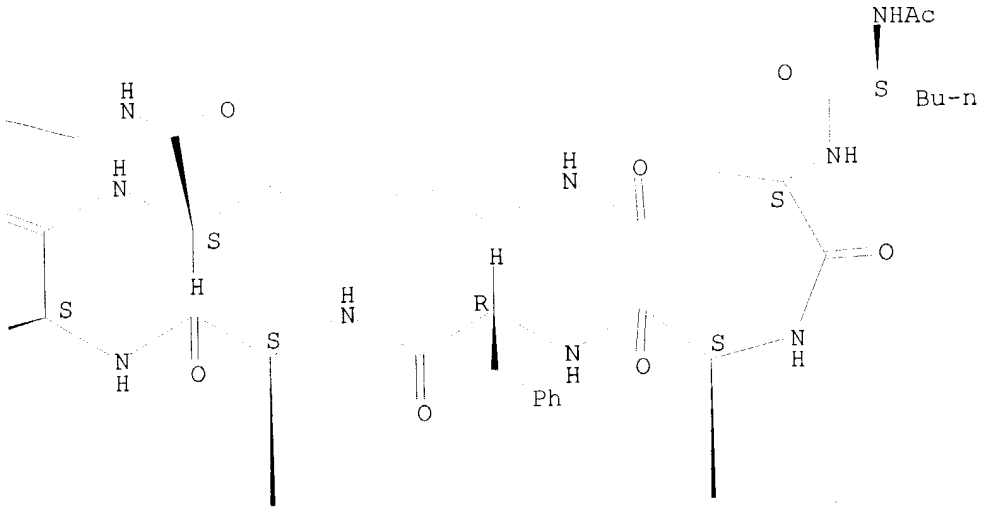
RN 122235-72-7 HCAPLUS
CN L-Valinamide, N-acetyl-L-norleucyl-L-α-aspartyl-L-histidyl-D-phenylalanyl-L-arginyl-L-tryptophyl-L-lysylglycyl-L-prolyl-, cyclic (2→7)-peptide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 2-B

Search completed by David Schreiber x22526